

Functions of Blood

- Transportation-
 - oxygen
 - carbon dioxide
 - waste
 - nutrients
 - hormones
- Regulation-
 - pH
 - temperature
 - influences water content of cells
- Protection-
 - blood loss via clotting mechanisms
 - foreign microbes via white cells

Physical Properties of Blood

- viscous fluid
 - viscosity is the resistance of a fluid to flow due to cohesion between its particles
- temperature is 38°C (100.4°F)
- pH range 7.35-7.45 (slightly alkaline)
- NaCl concentration of 0.9%
- volume in male, 5-6L, Female 4-5L
- 8% of the total body weight

General Properties of Whole Blood*

Fraction of body weight	8%
Volume in the adult body	Female: 4–5 L; male: 5–6 L
Volume/body weight	80–85 mL/kg
Mean temperature	38° C (100.4° F)
pH	7.35–7.45
Viscosity (relative to water)	Whole blood: 4.5–5.5; plasma: 2.0
Osmolarity	280–296 mOsm/L
Mean salinity (mainly NaCl)	0.9%
Hematocrit (percent RBCs by volume)	Female: 37%–48%; male: 45%–52%
Hemoglobin	Female: 12–16 g/dL; male: 13–18 g/dL
Mean RBC count	Female: 4.8 million/ μ L; male: 5.4 million/ μ L
Platelet count	130,000–360,000/ μ L
Total WBC count	5,000 - 10,000/ μ L

*Values may vary slightly depending on the testing methods used.

Components of Blood

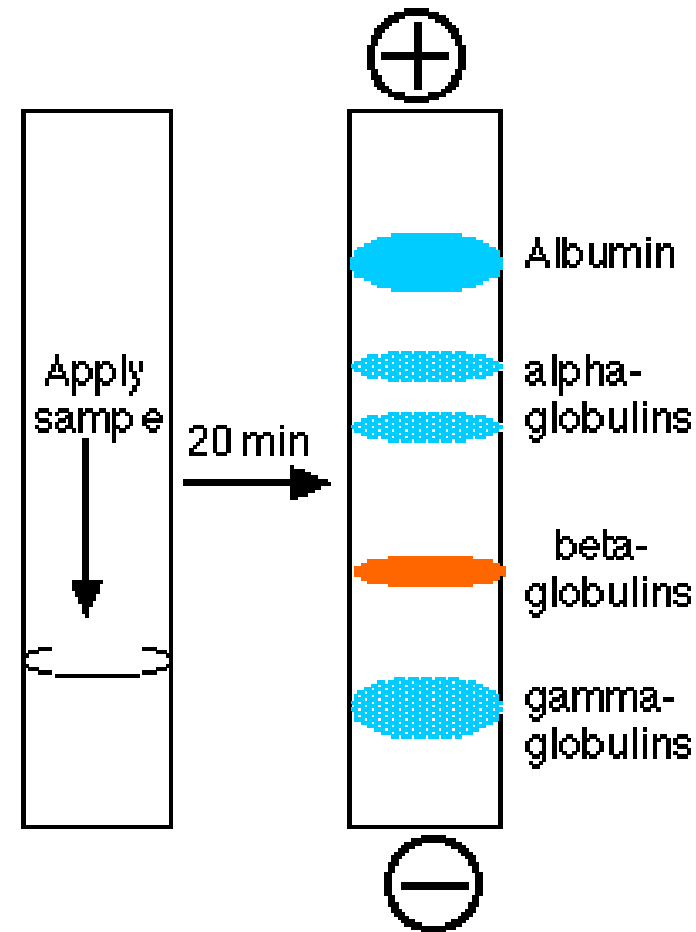
Formed Elements

- Erythrocytes (red blood cells)
- Leukocytes (white blood cells)
 - Granular leukocytes
 - neutrophils
 - eosinophils
 - basophils
 - Agranular leukocytes
 - lymphocytes
 - monocytes
- Platelets (thrombocytes)

Components of Blood

Plasma

- consist of 91.5% water and 8.5% solutes (proteins, nutrients, gases, electrolytes, waste products, enzymes, and hormones)
- plasma proteins- proteins found and confined only in the blood
 - **Albumins**- manufacture in the liver and is responsible for maintaining water balance in the blood.
 - Consist of 55% of the total plasma proteins
 - **Globulins**
 - proteins divided into 3 classes according to electrophoretic separation
 - - antibodies produced by certain white cells that functions in immunity.
 - 35% of total plasma proteins
 - **Fibrinogen**- soluble precursor of fibrin that functions in the blood clotting mechanisms along with platelets.



Separating serum proteins
by electrophoresis

Serum Globulins

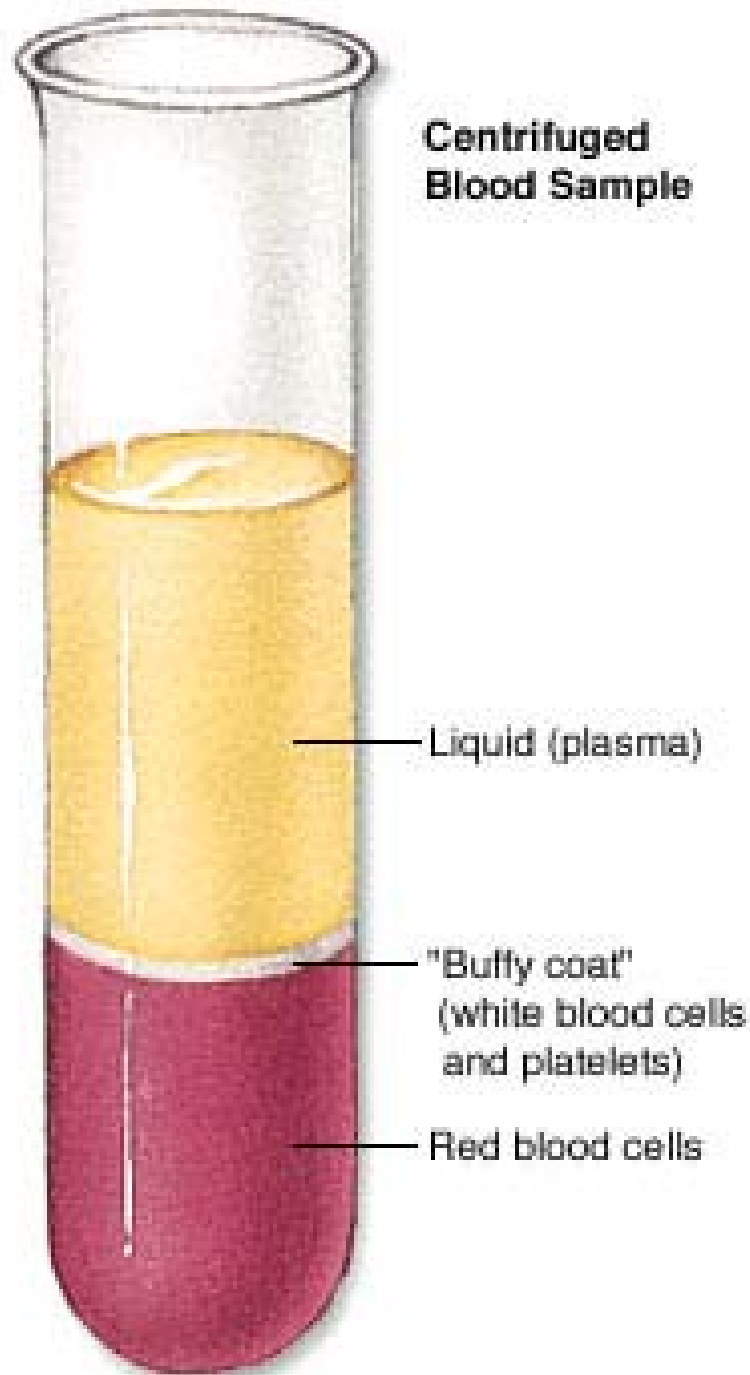
Alpha-Globulins

- alpha 1-Antichymotrypsin
- alpha 1-Antitrypsin
- alpha-Macroglobulins
- Antiplasmin
- Antithrombin III
- Ceruloplasmin
- Haptoglobins
- Heparin Cofactor II
- Orosomucoid
- Progesterone-Binding Globulin
- Retinol Binding Proteins
- Transcortin

Beta Globulin

- beta-2 Microglobulin
- beta-Thromboglobulin
- Hemopexin
- Plasminogen
- Properdin
- Sex Hormone-Binding Globulin
- Transferrin
- complement factor H

Centrifuged Blood Sample



Plasma is a pale yellow fluid that consists of about 92% water and 8% other substances, such as proteins, ions, nutrients, gases, and waste products.

Plasma is a colloidal solution, which is a liquid containing suspended substances that do not settle out of solution. Most of the suspended substances are plasma proteins, which include albumins, globulins, and fibrinogen.

Plasma volume remains relatively constant. Normally, water intake through the digestive tract closely matches water loss through the kidneys, lungs, digestive tract, and skin.

Monocyte

Platelets

Small lymphocyte

Neutrophil

Large lymphocyte

Basophil

Small lymphocyte

Neutrophil

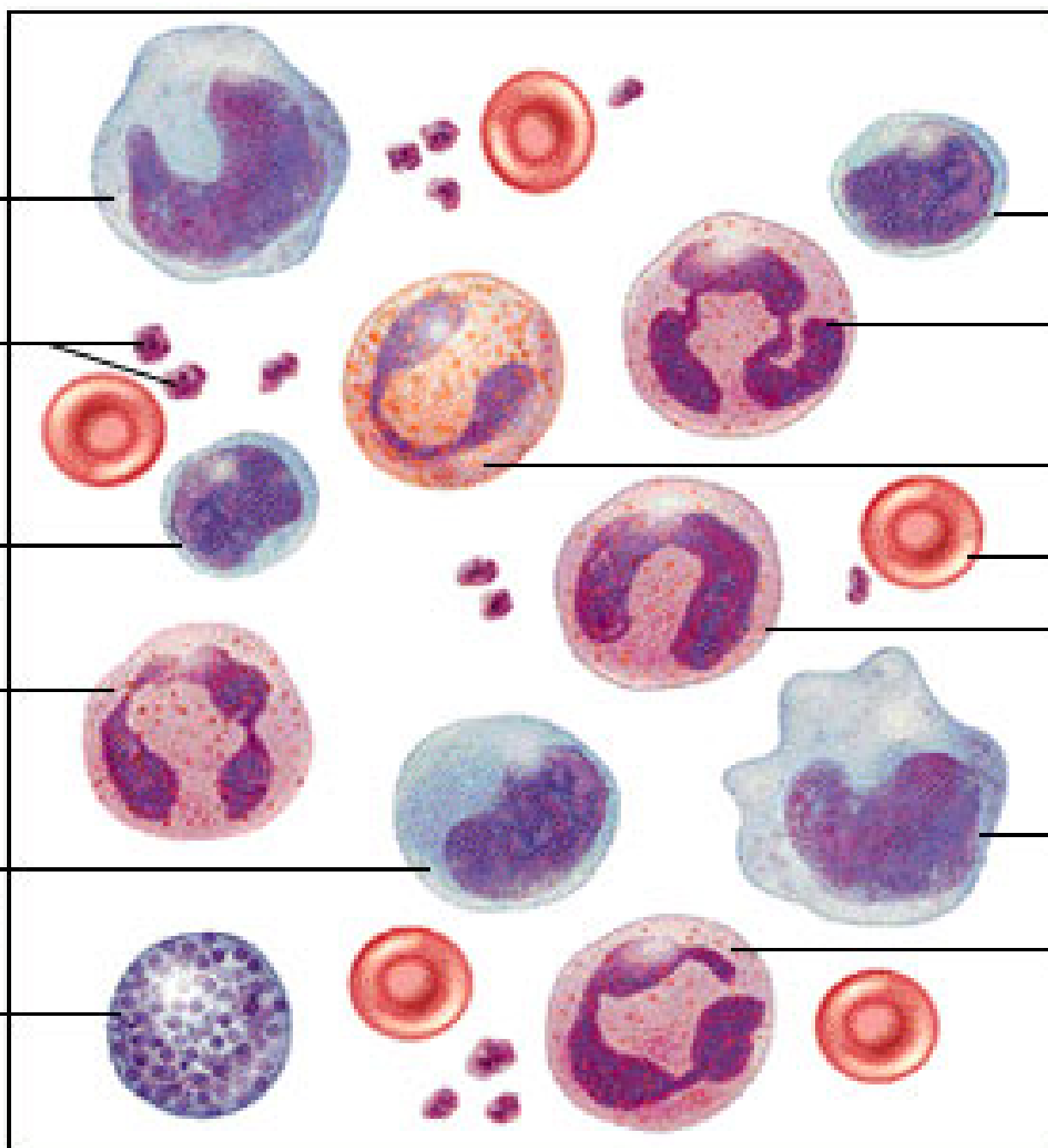
Eosinophil

Erythrocyte

Young (band) neutrophil

Monocyte

Neutrophil

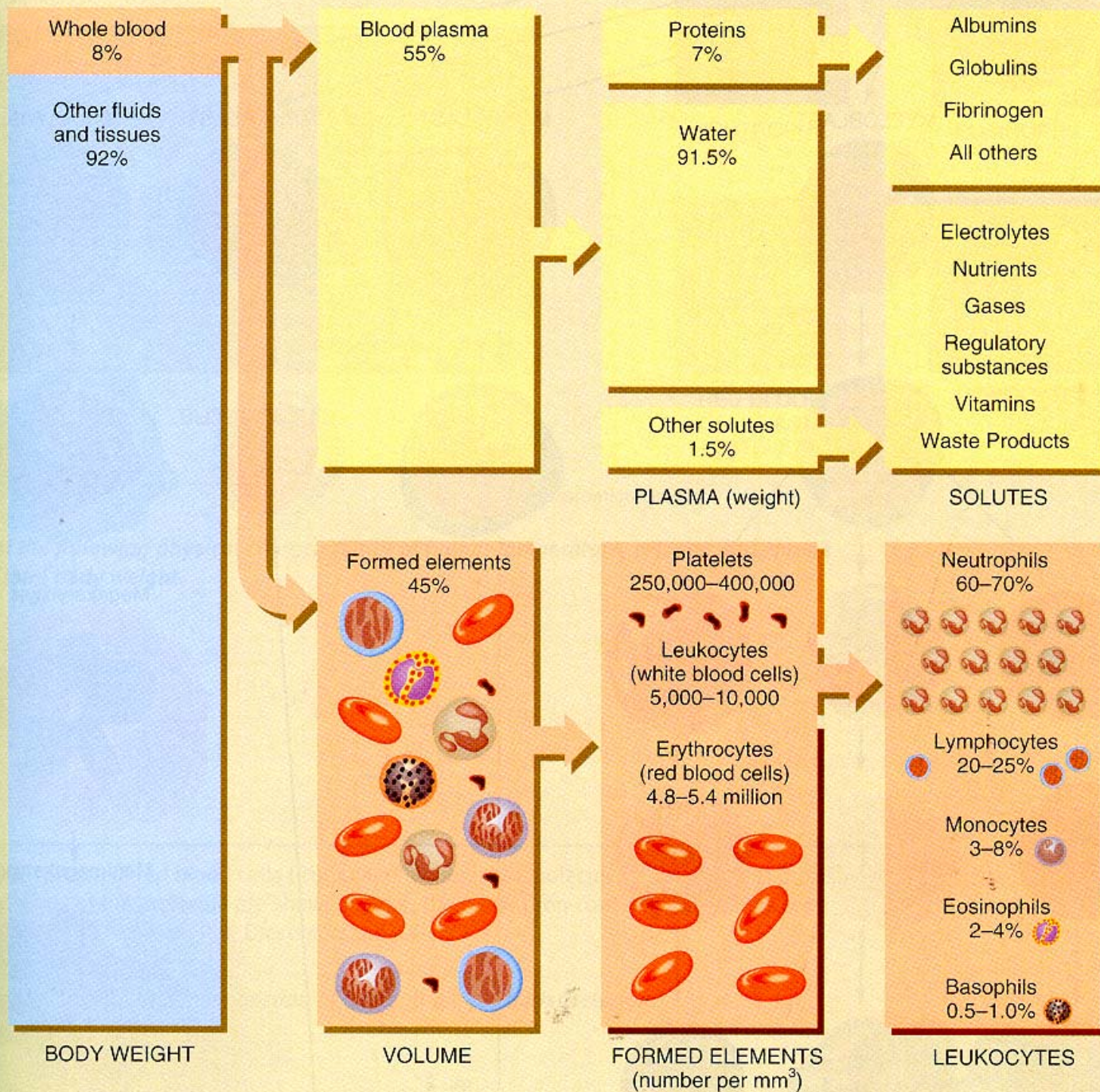


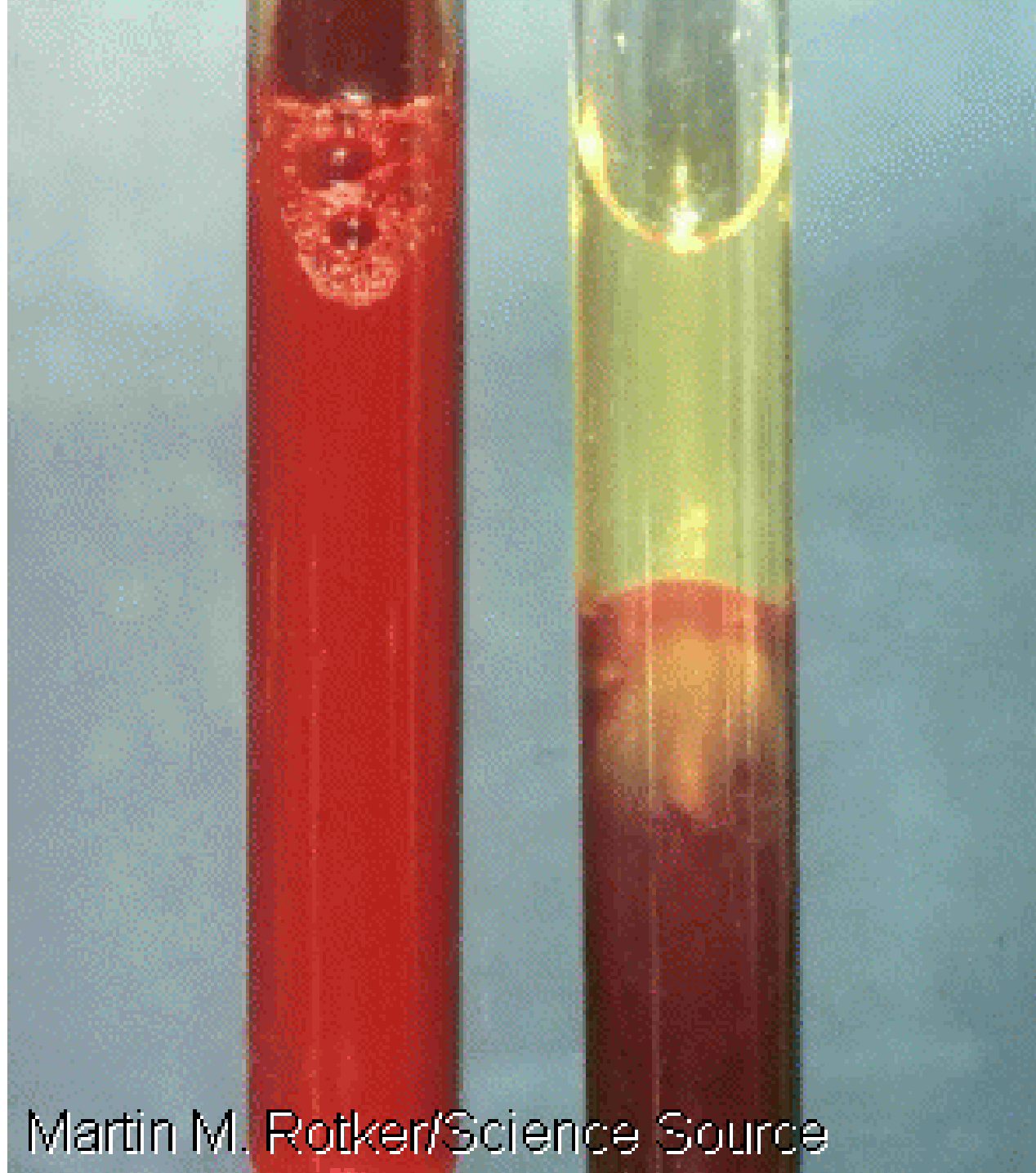
The Formed Elements of Blood

Plasma	Function	Source
Water (90–92% of plasma)	Maintains blood volume; transports molecules	Absorbed from intestine
Plasma proteins (7–8% of plasma) Albumins Fibrinogen Globulins	Maintain blood osmotic pressure and pH Maintain blood volume and pressure; transport Clotting Transport; fight infection	Liver Liver Liver Liver and plasma cells
Salts (less than 1% of plasma) Gases Oxygen Carbon dioxide nitrogen	Maintain blood osmotic pressure and pH; aid metabolism Cellular respiration End product of metabolism	Absorbed from intestinal villi Lungs Tissues
Nutrients Fats Glucose Amino acids	Food for cells	Absorbed from intestinal villi
Nitrogenous waste Urea Uric acid		Liver
Other Hormones, vitamins, etc.	Aid metabolism	Varied

Plasma Proteins

Protein	Percentage of Total	Origin	Function
<i>Albumin</i>	60%	Liver	Helps maintain blood osmotic pressure; transports lipids, hormones, and other solutes; helps maintain plasma pH
<i>Globulin</i>	36%		
Alpha globulins		Liver	Transport lipids and fat-soluble vitamins and aid in blood clotting
Beta globulins		Liver	Transport lipids and fat-soluble vitamins
Gamma globulins		Plasma cells	Constitute a type of antibody
<i>Fibrinogen</i>	4%	Liver	Blood coagulation





Martin M. Rotker/Science Source

Red blood cell indices

- Are measurements that describe the size and oxygen-carrying protein (hemoglobin) content of red blood cells.
- The indices are used to help in the differential diagnosis of **anemia** (a person's blood cannot carry as much oxygen as it should).

Anemia

- A healthy person has an adequate number of correctly sized red blood cells that contain enough hemoglobin to carry sufficient oxygen to all the body's tissues.
- **An anemic person has red blood cells that are either too small or too few in number.**
 - As a result, the heart and lungs must work harder to make up for the lack of oxygen delivered to the tissues by the blood.
- Anemia is caused by many different diseases or disorders. The first step in finding the cause is to determine what type of anemia the person has. **Red blood cell indices help to classify the anemias.**

Anemia (cont)

- Anemia has several general causes:
 - blood loss
 - Blood loss can result from severe hemorrhage or a chronic slow bleed, such as the result of an accident or an ulcer.
 - a drop in production of red blood cells
 - Lack of **iron**, **vitamin B12**, or **folic acid** in the diet, as well as certain chronic diseases, lower the number of red blood cells produced by the bone marrow.
 - a rise in the number of red blood cells destroyed.
 - Inherited disorders affecting hemoglobin, severe reactions to blood transfusions, prescription medications, or poisons can cause red blood cells to burst (hemolyze) well before the end of their usual 120-day lifespan.

- Anemia of any type affects the results of one or more of the common blood tests. These tests are the
 - **hematocrit**,
 - hemoglobin
 - red blood cell count
 - The hematocrit is a measure of red blood cell mass, or how much space in the blood is occupied by red blood cells. The **hemoglobin test** is a measure of how much hemoglobin protein is in the blood. The red blood cell count (RBC) measures the number of red blood cells present in the blood. Red blood cell indices are additional measurements of red blood cells based on the relationship of these three test results.

Red Blood Cell Indices

Red blood cell count (RBC)

- measures the number of red blood cells present in the blood.

Mean corpuscular volume (MCV)

- It measures the average volume of a red blood cell by dividing the hematocrit by the RBC.
- The MCV categorizes red blood cells by size.
 - cells of normal size are called **normocytic**
 - smaller cells are **microcytic**
 - larger cells are **macrocytic**

Red cell distribution width (RDW)

- measures the variation in size of the red blood cells.
- Usually red blood cells are a standard size. Certain disorders, however, cause a significant variation in cell size.

Red blood cell indices

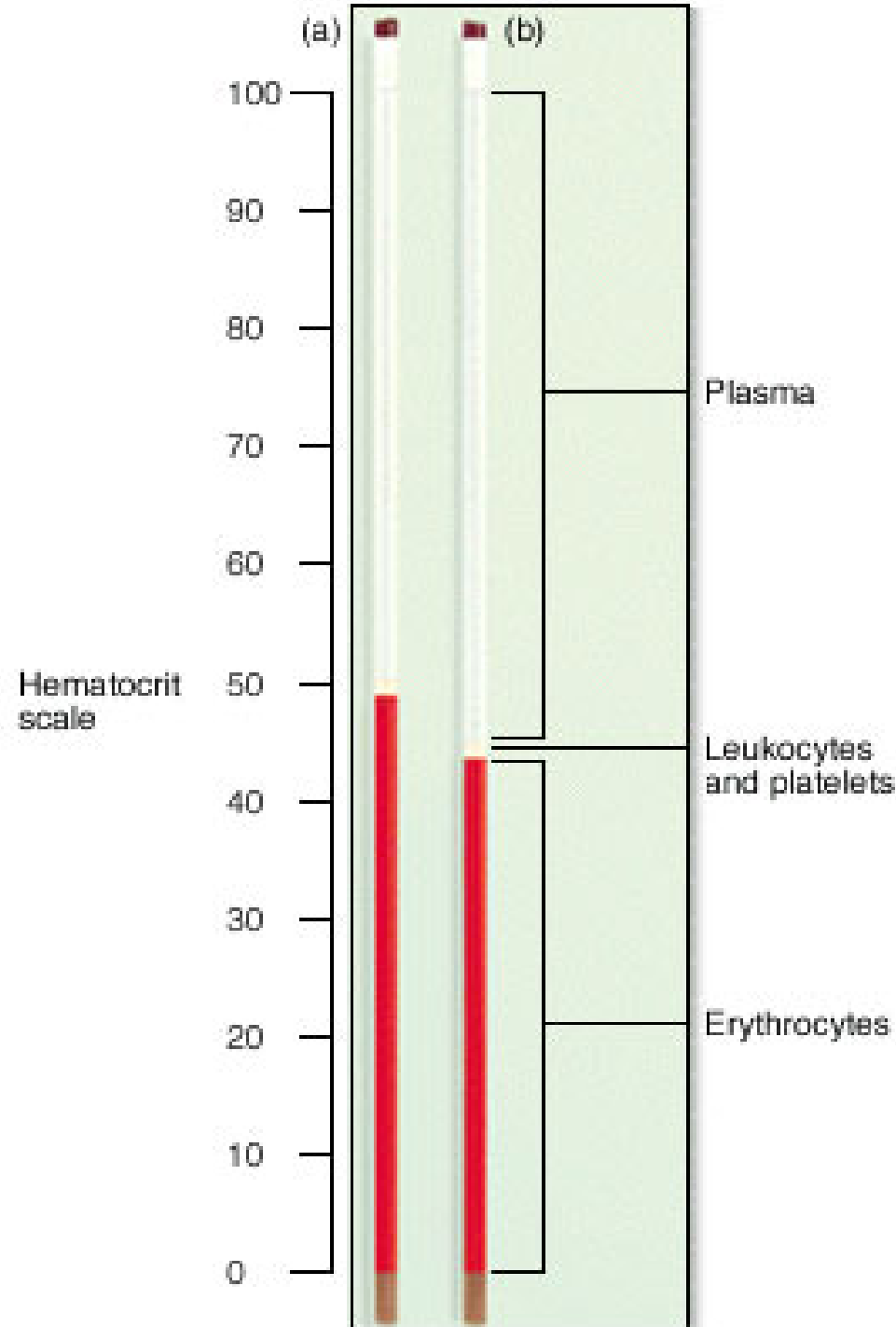
Hematocrit- a measure of red blood cell mass, or how much space in the blood

- is the percentage of whole blood volume composed of RBCs

Normal hematocrits of male (a) 42-52% and female (b) 37-48%.

Blood is separated into plasma, erythrocytes, and a small amount of leukocytes and platelets, which rest on the erythrocytes.

The hematocrit measurement includes only the erythrocytes and does not measure the leukocytes and platelets.

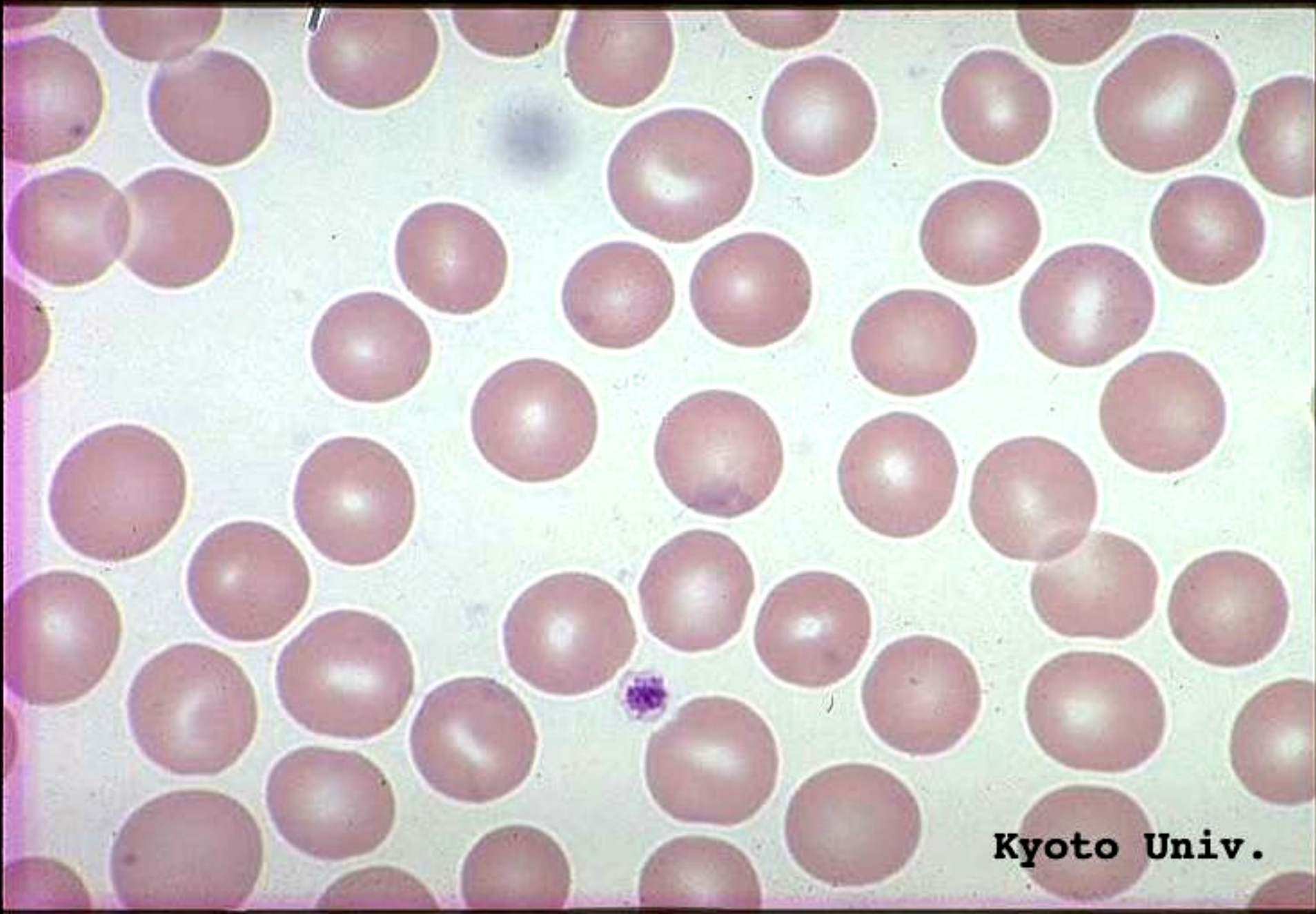


Red blood cell indices (cont)

Hemoglobin test is a measure of how much hemoglobin protein is in the blood.

- The **MCHC** (mean corpuscular hemoglobin concentration) measures the average concentration of hemoglobin in a red blood cell.
 - calculated by dividing the hemoglobin by the hematocrit.
- Categorizes red blood cells according to their concentration of hemoglobin.
 - Cells with a normal concentration of hemoglobin are called **normochromic**.
 - When examined under a microscope, normal red blood cells that contain a normal amount of hemoglobin stain pinkish red with a paler area in the center.

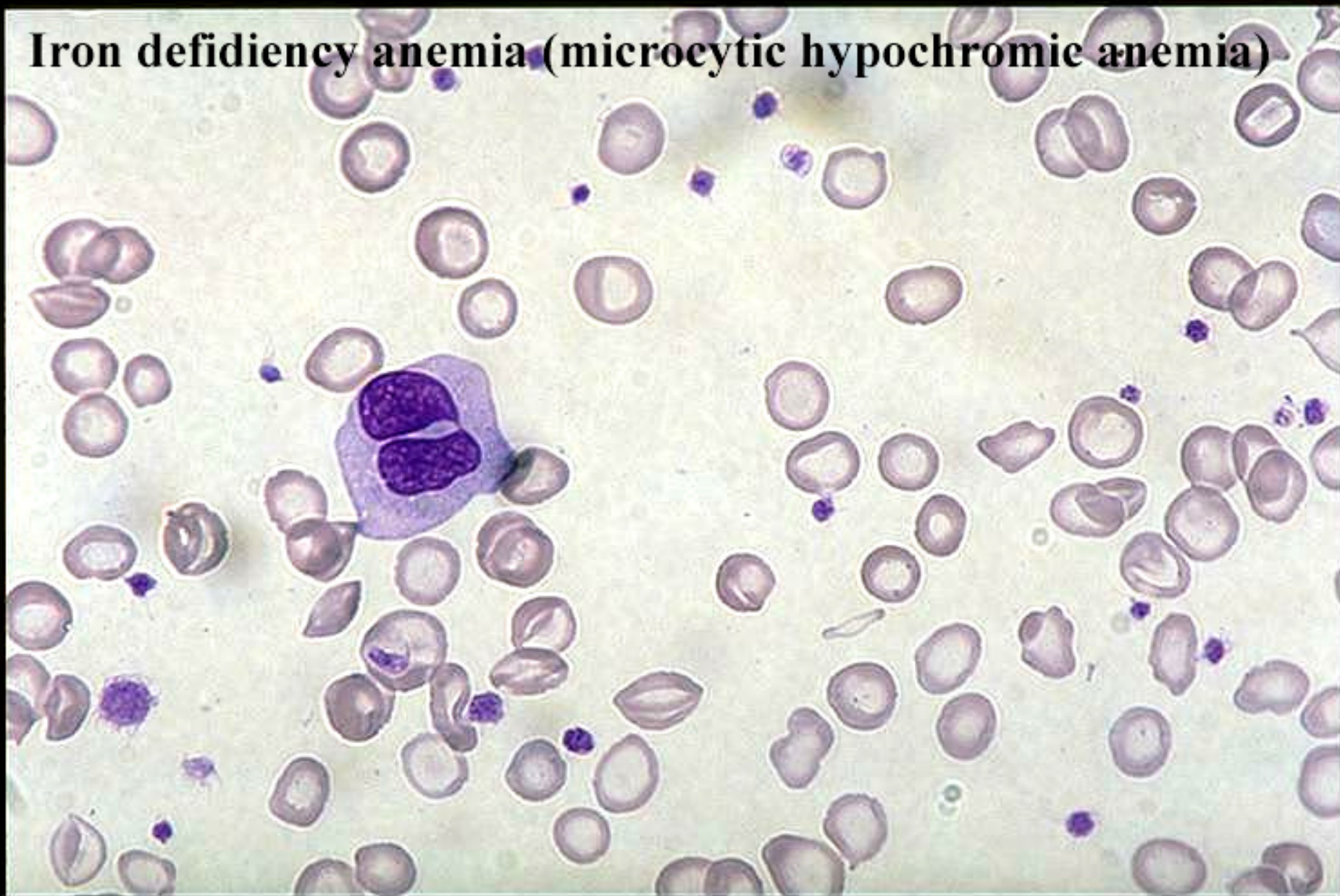
Normal Blood Smear



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- Categorizes red blood cells according to their concentration of hemoglobin (cont).
 - cells with a lower than normal concentration are called **hypochromic**.
 - Cells with too little hemoglobin are lighter in color with a larger pale area in the center.
- Because there is a physical limit to the amount of hemoglobin that can fit in a cell, there is no hyperchromic category.

Iron deficiency anemia (microcytic hypochromic anemia)



Formation of Blood

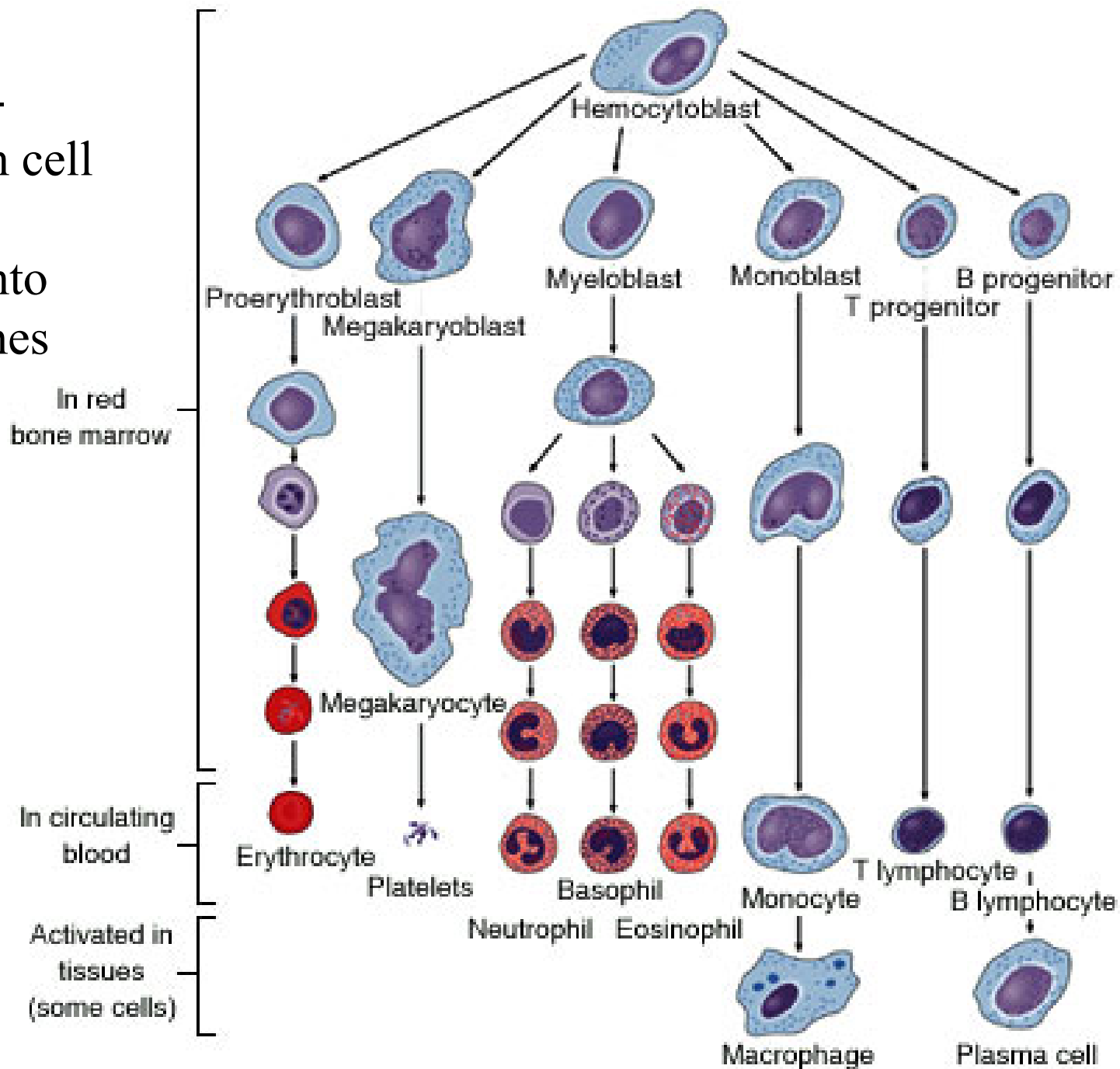
Hematopoiesis- the process by which blood cells are formed.

- In embryo there are multiple sites for blood formation
 - liver, spleen, thymus gland, lymph nodes, and red bone marrow
- after birth blood production takes place in the red bone marrow of various long and flat bones.
 - Femur, humerus, sternum, ribs, vertebrae, and cranial bones
- All blood cells originate from hemopoietic stem cells
 - these cells differentiate into the five types of blood cells:
 - erythrocytes
 - granulocytes- eosinophils, neutrophils, basophils
 - monocytes
 - lymphocytes
 - platelets

} agranulocytes

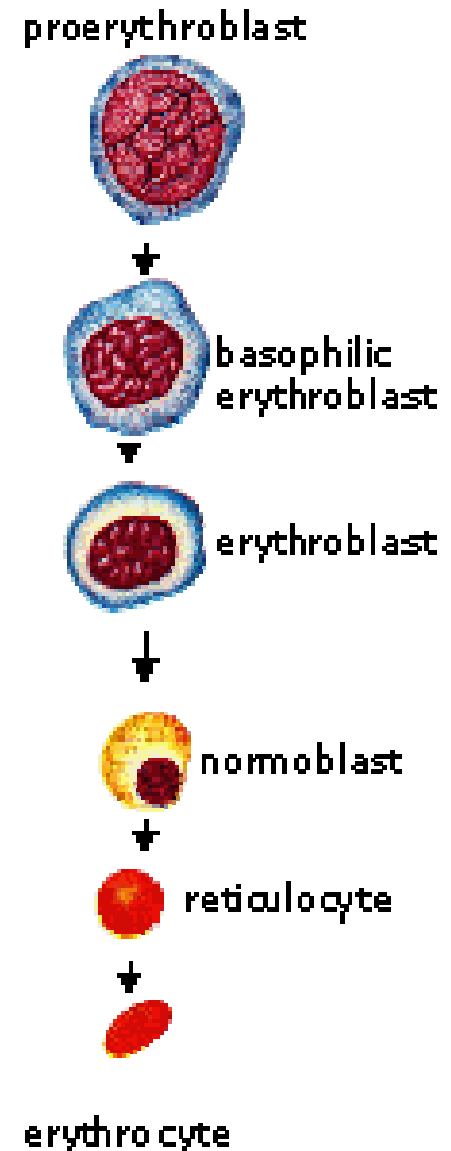
Hemocytoblast-
multipotent stem cell
capable of
differentiating into
multiple cells lines

- Red cells
- White cells
- Platelets



Erythropoiesis

- Proerythroblast is the first committed cell, having receptors for the hormone erythropoietin (EPO)
 - secreted by the kidney that stimulates proerythroblast to mature into erythroblast
- Erythroblast manufactures hemoglobin and then discards its nucleus which it is then called a reticulocyte (distinguished by its network of endoplasmic reticulum)
 - takes 3-4 days
- Reticulocytes enter the blood stream, eventually lose their ER, then become mature erythrocytes



Erythropoiesis (cont.)

- About .5-1.5% of the circulating RBCs are reticulocytes
- Percentage increases under certain circumstances
 - diseases where blood is destroyed prematurely
 - spending extended amounts of time at high elevations
 - blood loss
 - these conditions stimulate acceleration of RBC production where the bone is in such a hurry to replenish the lost RBCs that it lets many developing RBCs into circulation a little early
- **Reticulocyte count** is a blood test that measures how rapidly immature red blood cells are made by the bone marrow and then released into the blood.
 - Determines whether anemia is being caused by decreased production of red blood cells or by increased destruction (or loss) of red blood cells. The increased destruction or loss of red blood cells causes the bone marrow to make more reticulocytes.
 - Monitors treatment for anemia. For example, a higher reticulocyte count indicates that iron replacement treatment or other treatment to reverse the anemia is effective.

Erythropoiesis (cont.)

- The reticulocyte count is usually given as the percentage of red blood cells that are reticulocytes (the number of reticulocytes divided by the total number of red blood cells, multiplied by 100).
 - Normal: 0.5%–2.0%
 - Newborns have a normal reticulocyte count of 2.5% to 6.5%. This value drops within 2 weeks to 0.5% to 2.0%.

Erythropoiesis (cont.)

High values

- A high reticulocyte count may indicate
 - increased production of red blood cells by the bone marrow, which can be caused by bleeding,
 - a move to high elevation,
 - or certain types of anemia resulting in increased destruction of red blood cells (hemolysis).
- The reticulocyte count usually rises after successful treatment for pernicious anemia, iron-deficiency anemia, or folic acid deficiency anemia.

Erythropoiesis (cont.)

Low values

- A low reticulocyte count may indicate
 - decreased production of red blood cells by the bone marrow, which can be caused by aplastic anemia or other types of anemia, such as iron-deficiency anemia.
 - exposure to radiation,
 - a long-term (chronic) infection,
 - certain medications that damage the bone marrow.

Erythropoiesis (cont.)

- Reticulocyte index (RI)- a measurement that corrects the reticulocyte count for anemia, giving a more accurate picture of reticulocyte count.

Ex: In anemia, the reticulocyte count will be inaccurate because the levels of red blood cells and hemoglobin are decreased, which makes the reticulocyte count appear falsely high.

Red Blood Cells

Structure

- biconcave disc
- no nucleus or other organelles
- no mitosis and minimal metabolic activity
 - only cell in the body that carries out anaerobic fermentation indefinitely
- has the red pigment called **hemoglobin** that carries oxygen
- cell surface has antigens responsible for the various blood types (ABO and Rh)
- inner membrane surface has the proteins, **spectrin** and **actin**, that gives the membrane resilience and durability that is need as they squeeze through capillaries

Function

- hemoglobin combines with oxygen and carbon dioxide (5%)
 - globin- 4 proteins chains (two alpha and two beta chains)
 - heme- 4 nonprotein pigments and iron
 - oxygen attaches to iron

Normal Hemoglobins

- **Hemoglobin A-** This is the designation for the normal hemoglobin that exists after birth. Hemoglobin A is a tetramer with two alpha chains and two beta chains ($\alpha_2\beta_2$).
- **Hemoglobin A2-** This is a minor component of the hemoglobin found in red cells after birth and consists of two alpha chains and two delta chains ($\alpha_2\delta_2$). Hemoglobin A2 generally comprises less than 3% of the total red cell hemoglobin.
- **Hemoglobin F-** Hemoglobin F is the predominant hemoglobin during fetal development. The molecule is a tetramer of two alpha chains and two gamma chains ($\alpha_2\gamma_2$).
 - it binds oxygen more tightly , thus it enables the fetus to extract oxygen from the mother's bloodstream.

Globin

Heme

8 μm

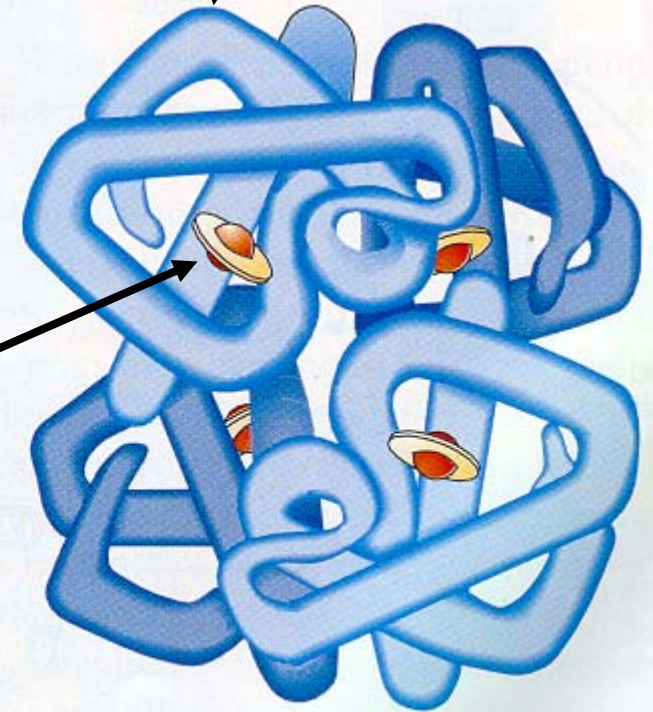


Surface view



Sectioned view

(a) RBC shape



(b) Hemoglobin molecule

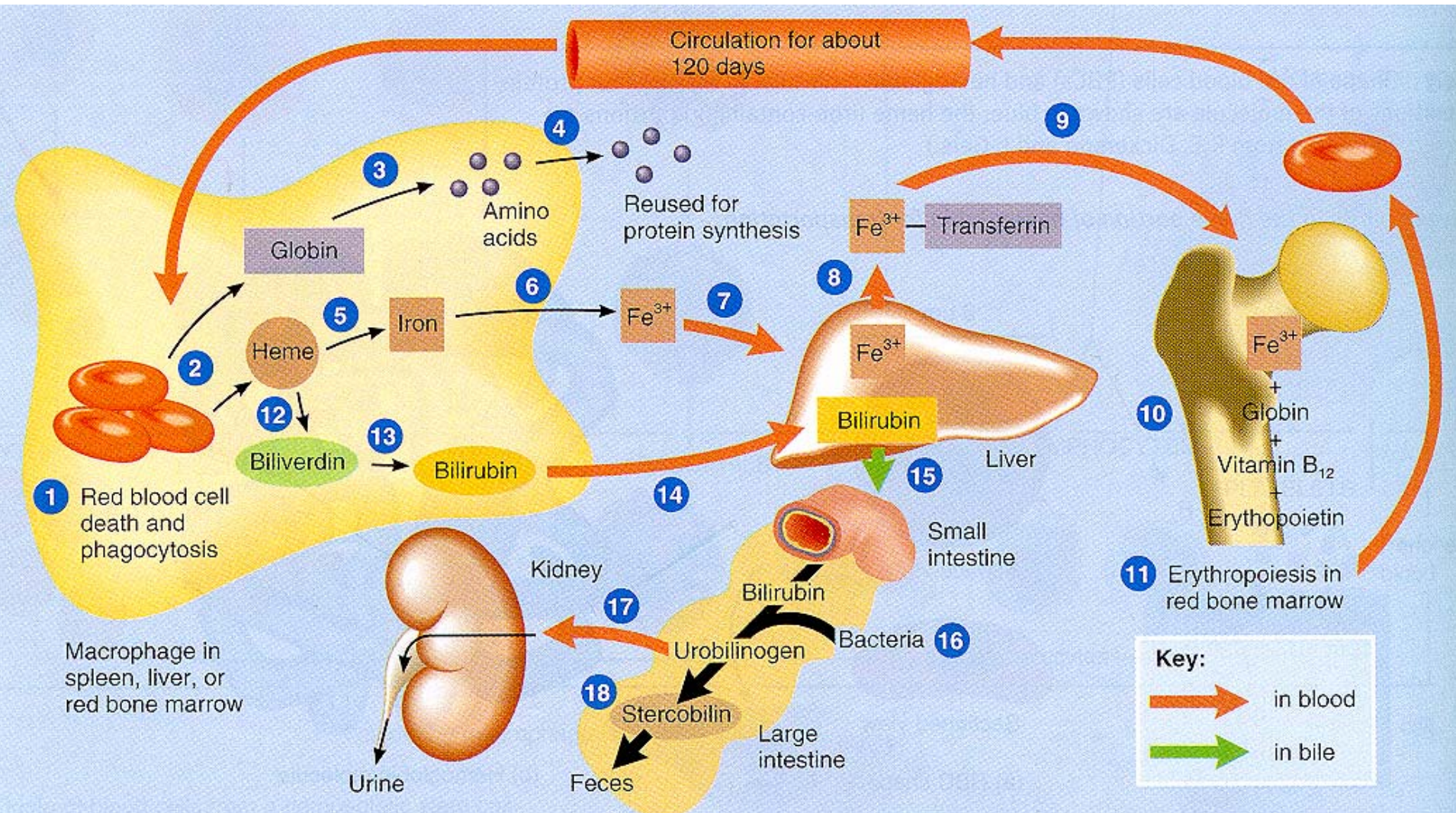
Key:

1 μm = 1/25,000 in.
or
1/10,000 cm
or
1/1000 mm

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Red Blood Cell Recycling



Jaundice- yellowish coloration of the eye and skin due to the increase in the blood concentration of bilirubin.

Neonatal Jaundice

RBC Production

Erythropoiesis- the process by which RBC's are formed.

Anemia- a decreased number of RBC's or hemoglobin.

Hypoxia- cellular oxygen deficiency.

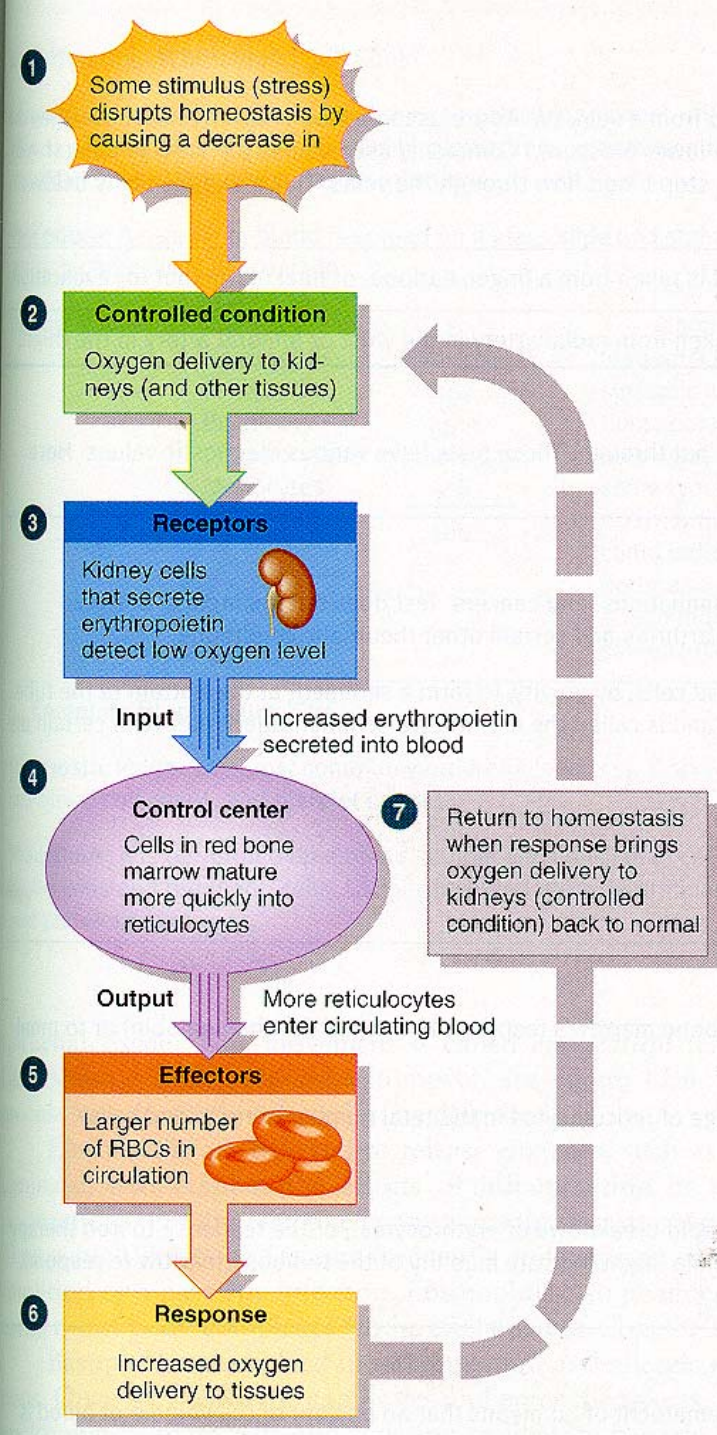
Cyanosis- bluish purple discoloration of the skin as a result of hypoxia.

Erythropoietin- hormone secreted from the kidney in response to hypoxia that acts on the bone marrow where it speeds the production of RBC's.

Intrinsic factor-secreted by gastric cells and needed for the absorption of B₁₂.

Iron

Folic acid



White Blood Cells (Leukocytes)

- Have nuclei
- Do not contain hemoglobin
- Function as part of the bodies immune system
- Grouped in to
 - Granular leukocyte
 - Agranular leukocyte

White Blood Cells (Leukocytes)

Granular leukocytes- have large granules in their cytoplasm and have bilobed nuclei.

- Three kinds
 - **neutrophils**- pale lilac-first responders to foreign invasion, phagocytic, release enzymes.
 - **eosinophils**- red orange-phagocyte, release enzymes that combat the effects inflammation in allergic reactions, and effective against parasitic infections.
 - **basophils**- blue-purple-release substances that are involved in inflammation and allergic reactions. Also called mast cells once in the tissue

White Blood Cells (Leukocytes)

Agranular leukocytes- cannot visible see granules (so described as agranular)

- **Lymphocytes-**
 - B cell- secretes antibody that is effective in destroying bacteria and deactivating toxins
 - T cells- attack viruses, fungi, transplanted tissue, and cancer cells
- **Monocytes-** most important phagocytic cell. Called macrophage when enter the tissue.

Emigration (Diapedesis)- the movement of cells out of the vascular system into the tissue

White Blood Cells

Major histocompatibility antigen- identification proteins on the cell surface of white cells and tissue cells.

Differential white blood cells count- a count of the number of kinds of white cells in a sample of 100 white cells.

WBC Life Span

- most live only a few days as compared to the 120 days of the red cell
- some B and T cells live for years

Leukocytosis- increase in the number of white cells.

Leukopenia- decrease in the number of white cells.

White Blood Cell Alterations

White Blood Cell Population Change

Illness

Elevated lymphocytes

Tuberculosis
Whooping cough

Elevated eosinophils

Parasitic infections such as:
Tapeworm infection
Hookworm infection

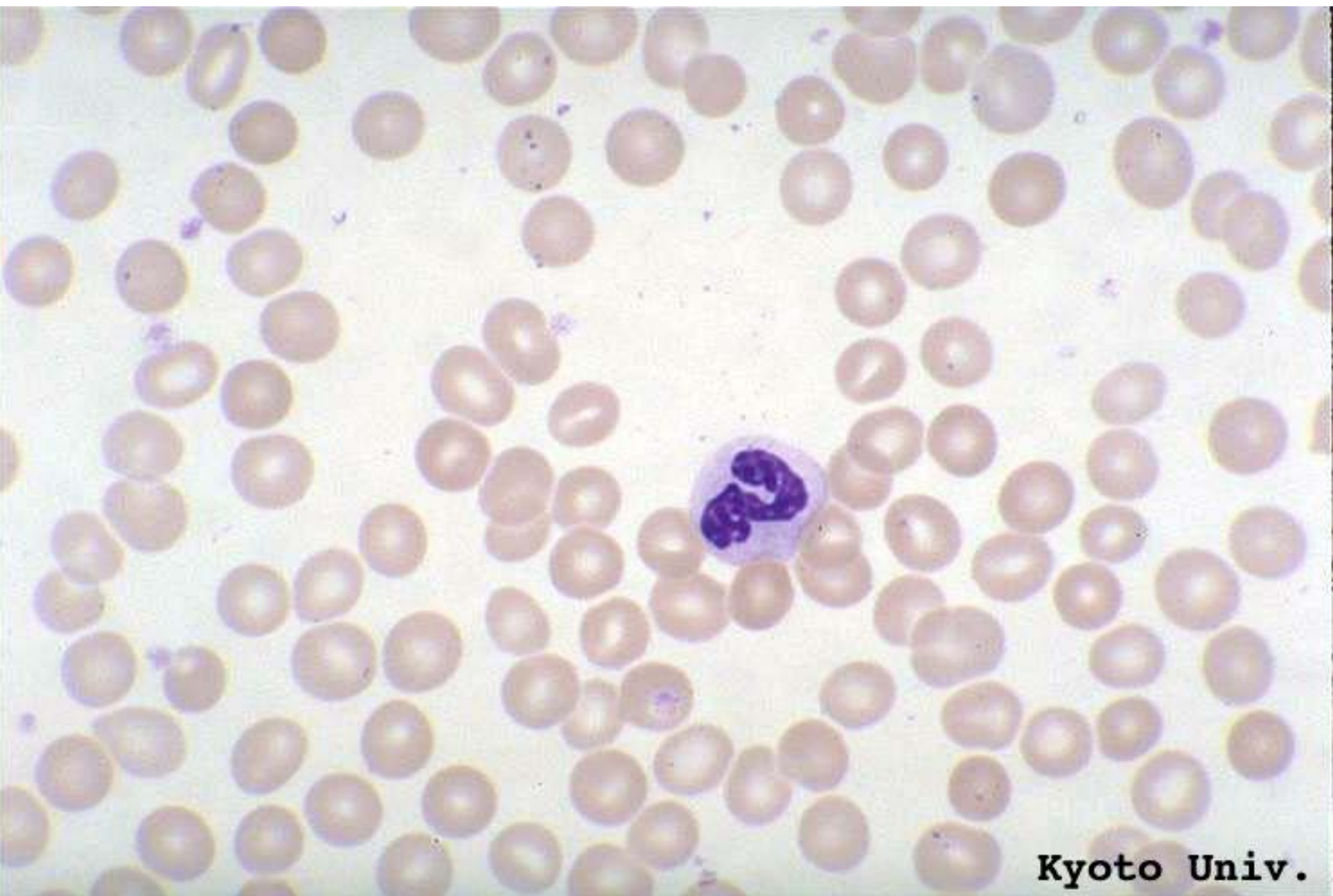
Elevated monocytes

Typhoid fever
Malaria
Mononucleosis

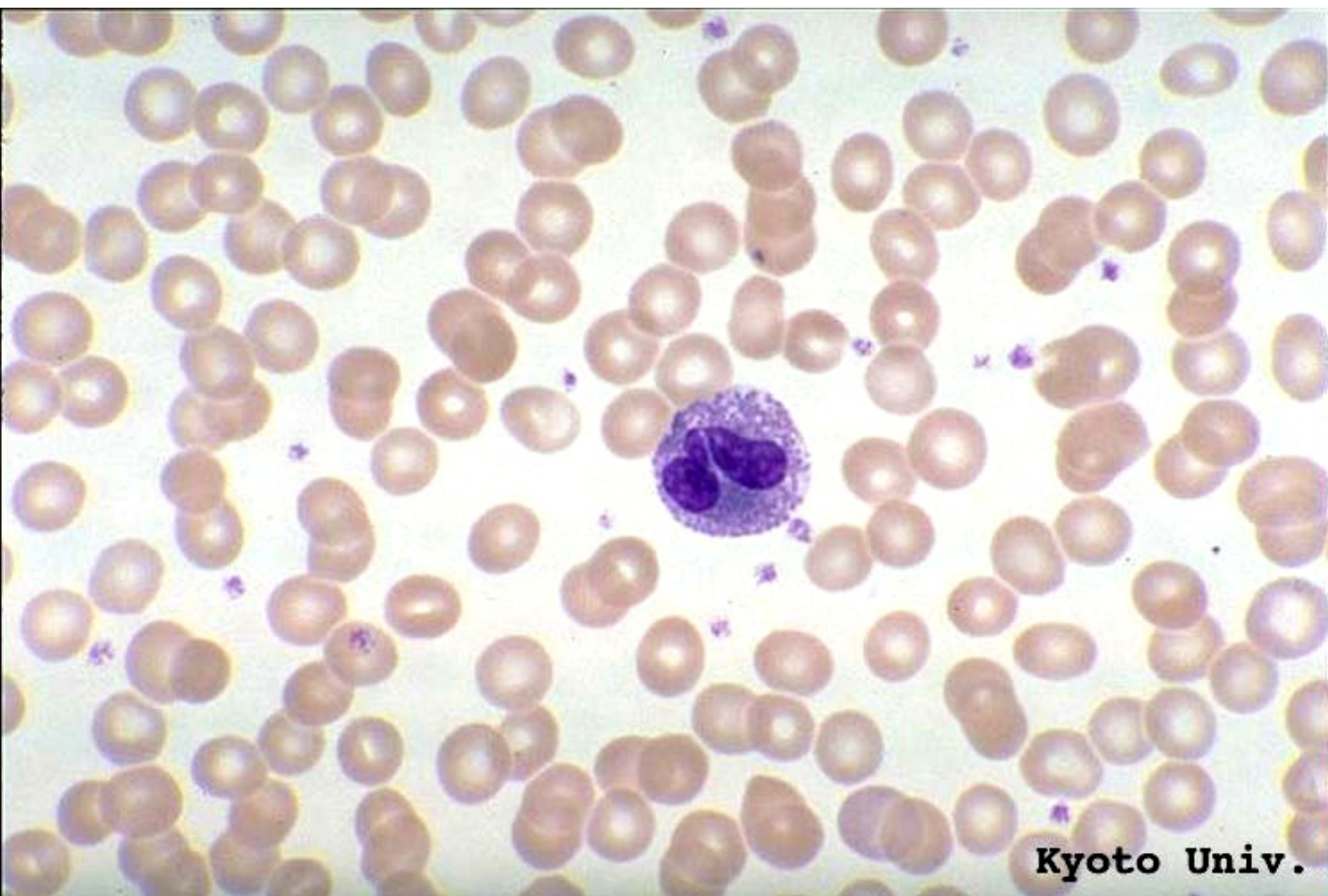
Too few helper T cells

AIDS

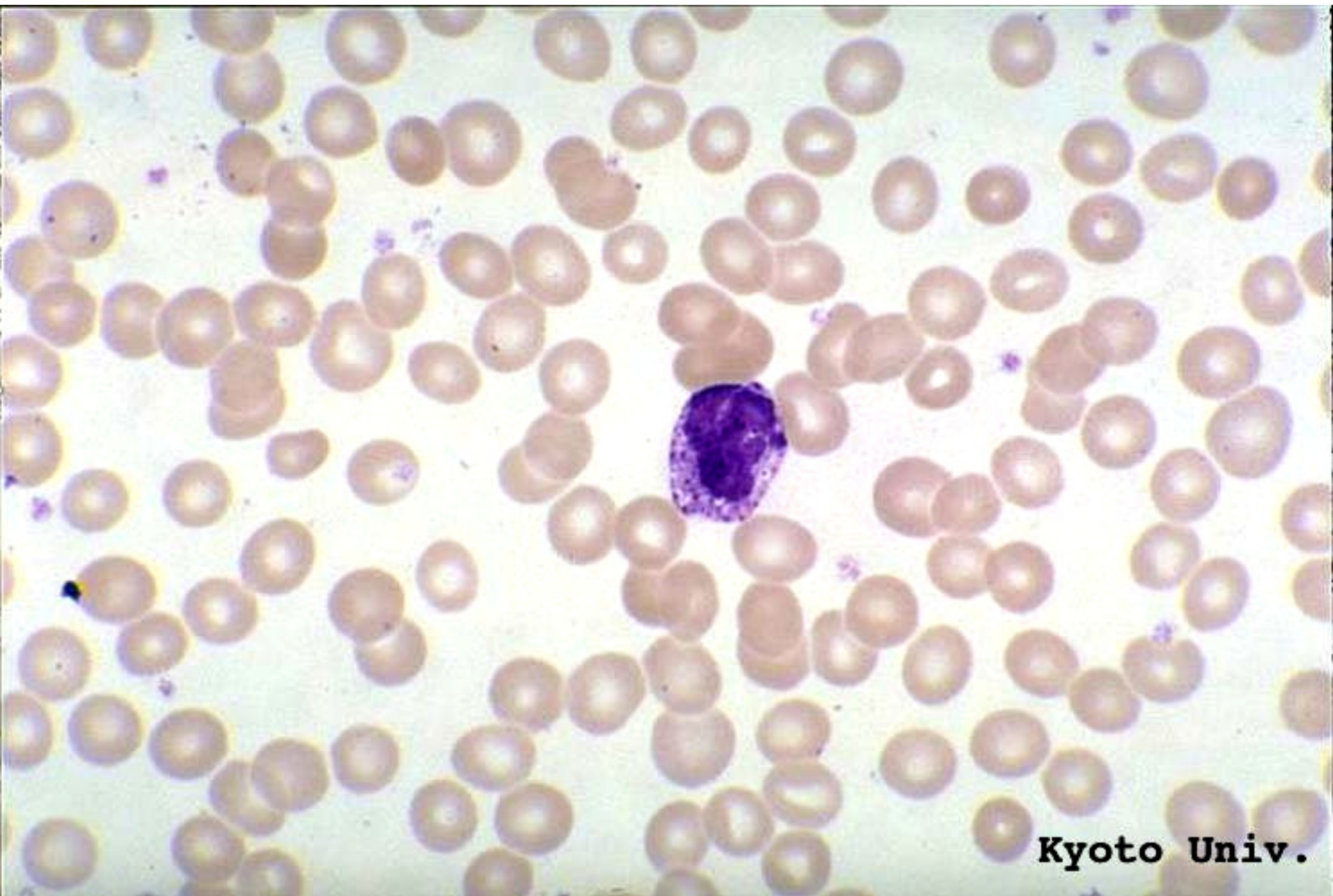
Neutrophil



Eosinophil

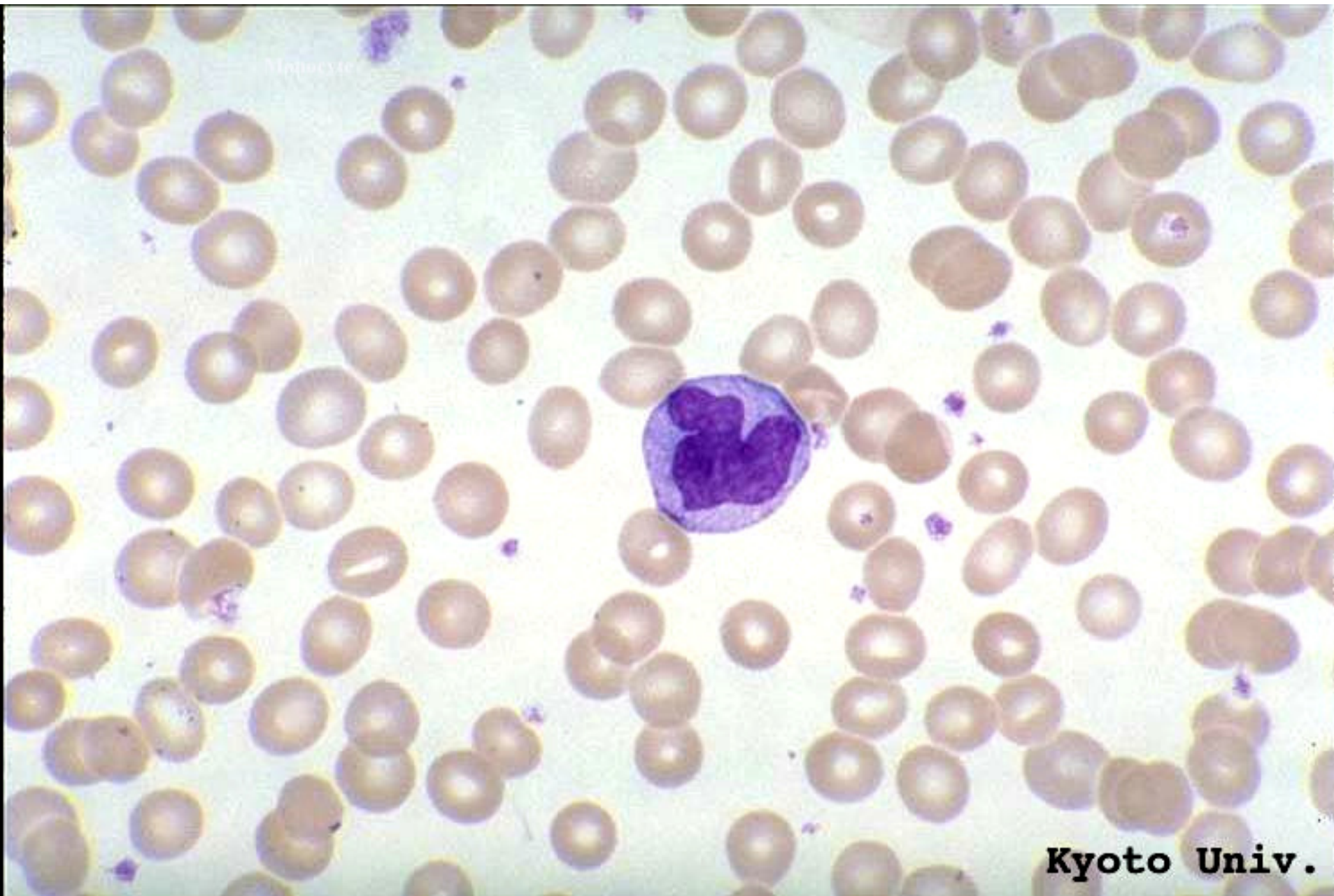


Basophil

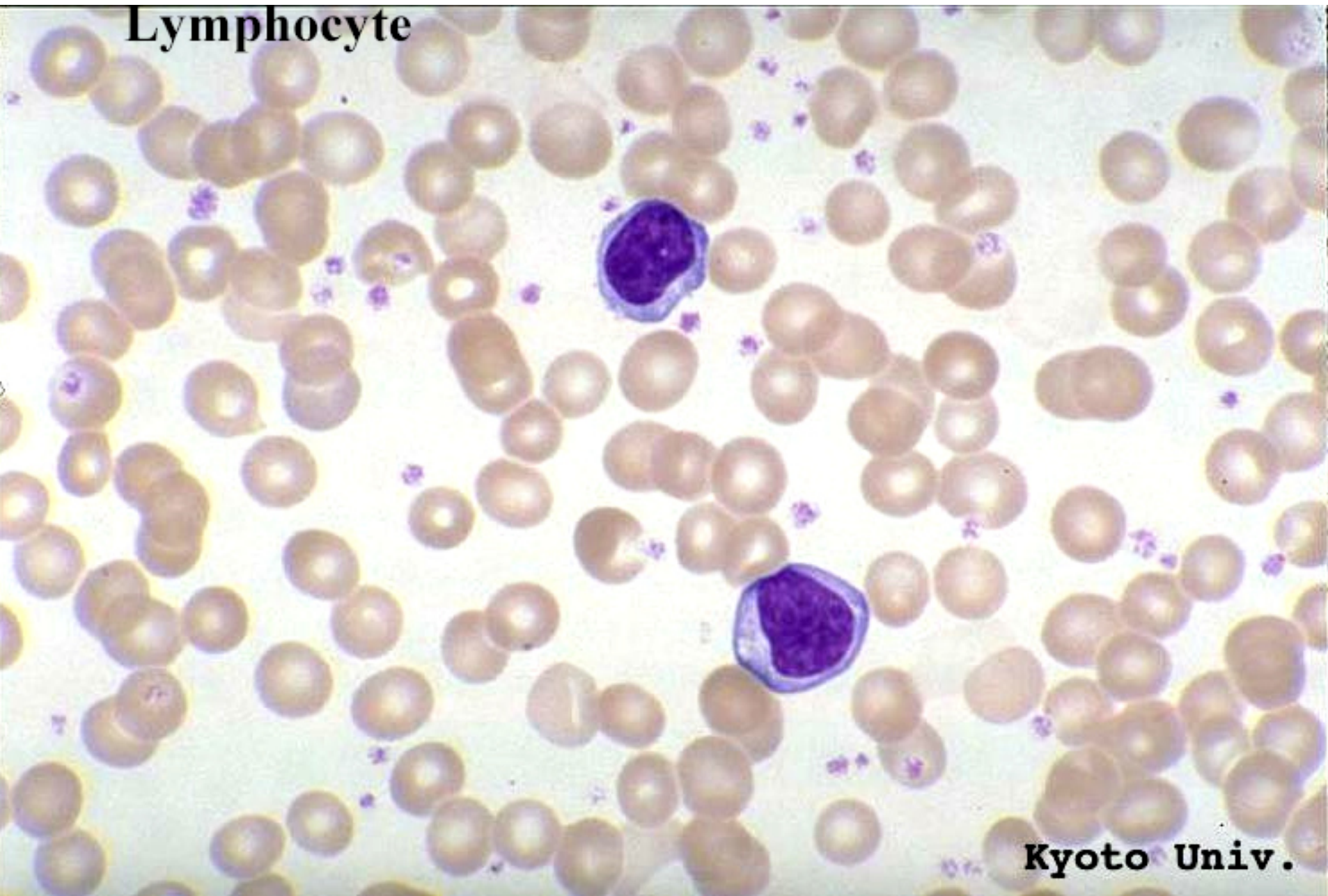


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Monocyte

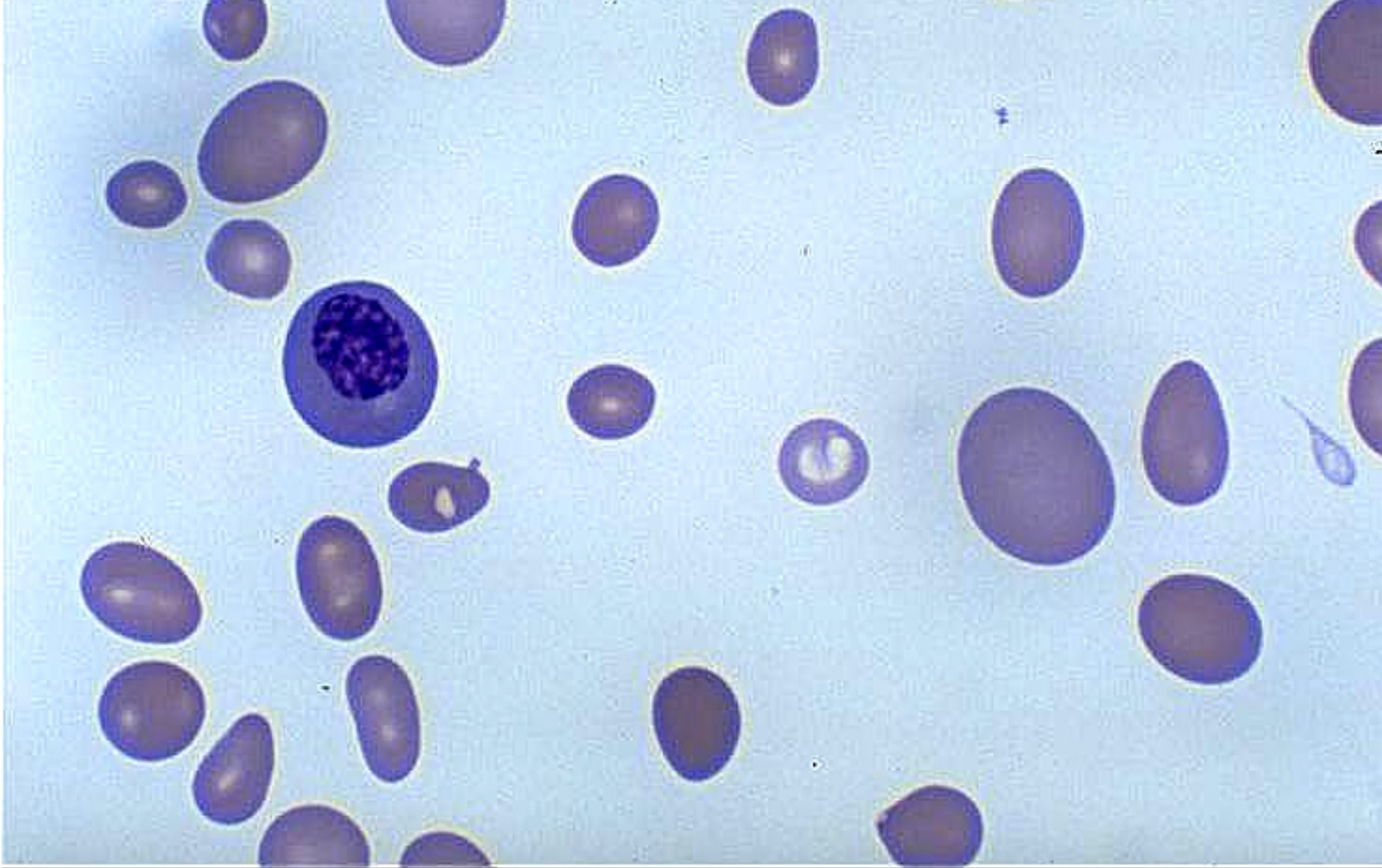


Lymphocyte

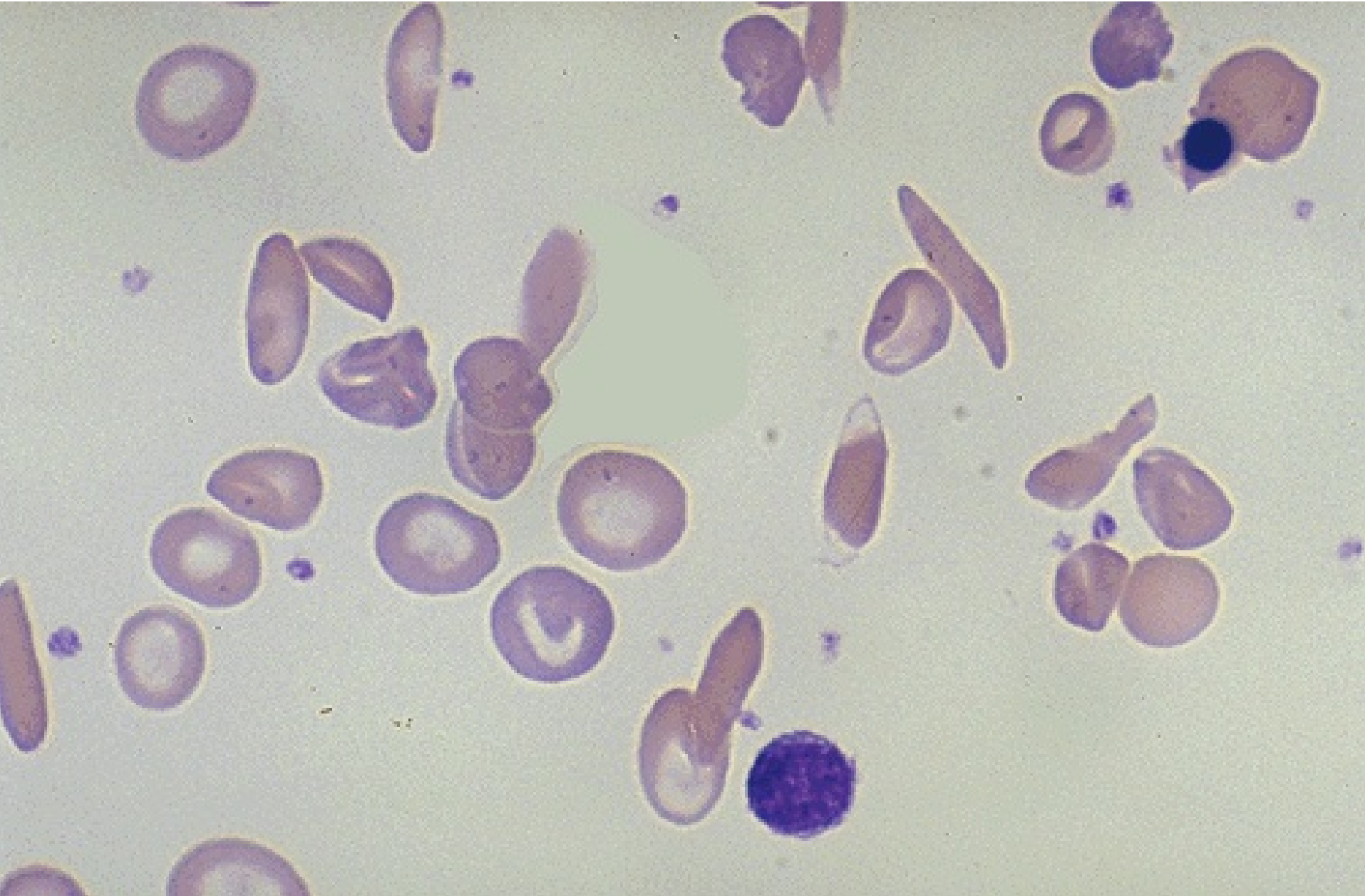


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B-12 Deficiency Anemia (megaloblastic anemia, macrocytic)



Sickle Cell Anemia



Platelets

- produced in the bone marrow
- are membrane enclosed fragments of the megakaryocyte
- involved in blood clotting mechanisms
- life span is 5 to 9 days

Plasma

- the liquid portion of blood
- consist of 91.5% water and 8.5% solute (plasma proteins, gases, electrolytes, waste products, enzymes, hormones)
- plasma proteins-
 - **Albumin**- manufactured in the liver and is responsible for maintaining blood volume. Comprise 55% of the plasma proteins.
 - **Globulins**- Comprise 38% of the plasma proteins. Produced by the lymphocytes (antibodies) and functions in immunity.
 - **Fibrinogen**- 7% of plasma proteins. Functions in blood clotting and is produced by the liver.

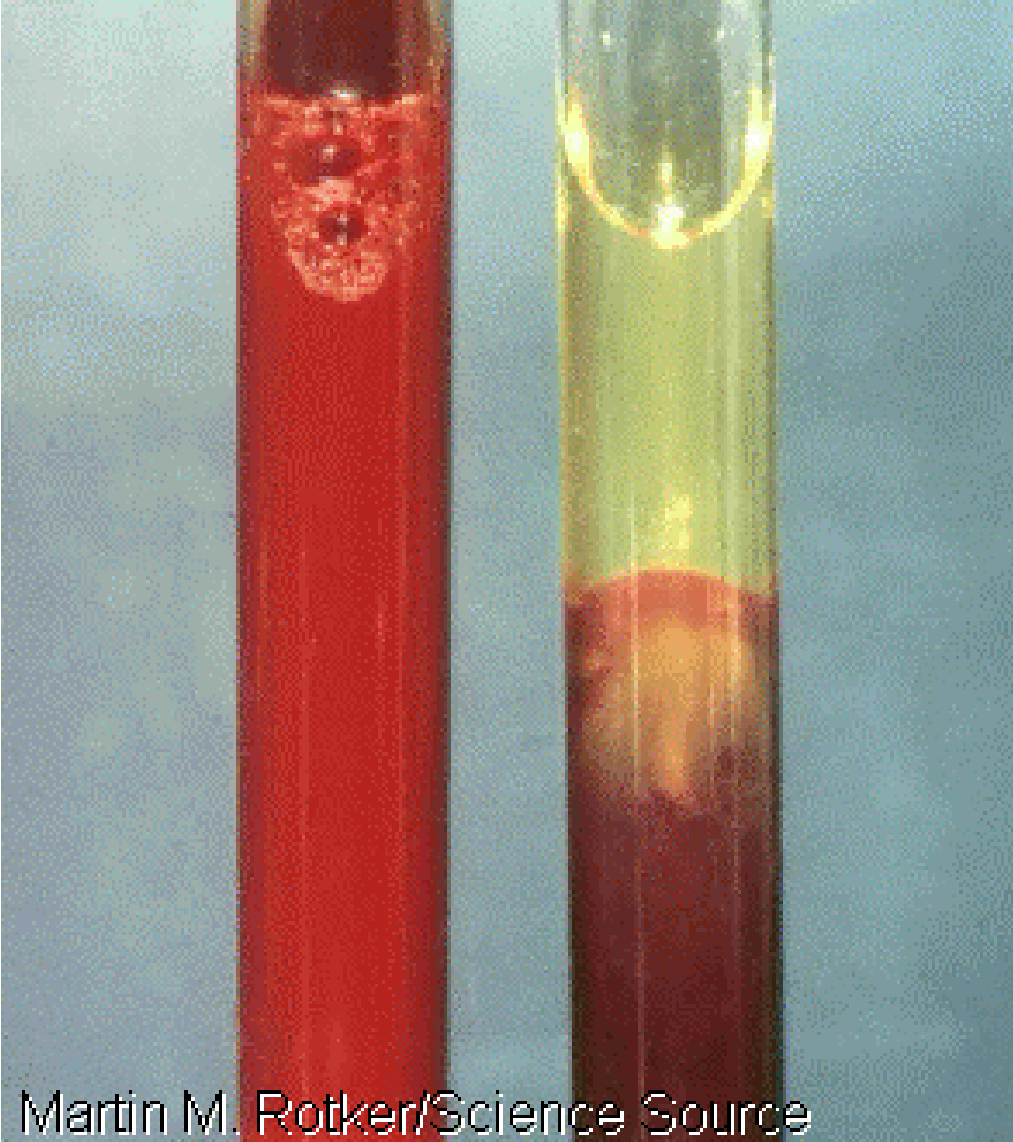
Hemostasis

The stoppage of bleeding

Three mechanisms

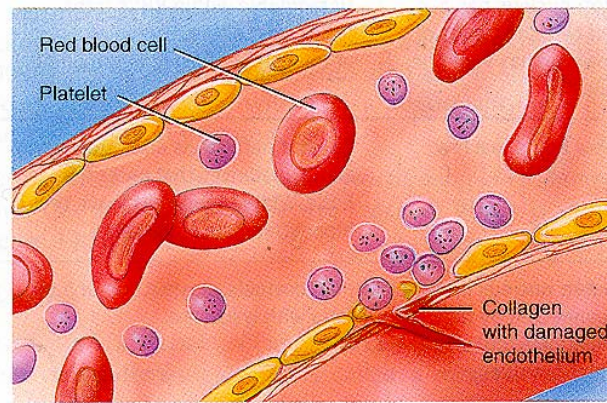
- **vascular spasm**- When the smooth muscle in the vascular wall contracts which serves to reduce blood flow to the damaged vessel.
- **platelet plug formation**- platelet contact with damaged vessel causes a series of reactions that results in massive platelet adhesion at site of damage (**platelet plug**). Is reinforced with fibrin threads during coagulation.
- **blood coagulation** (clotting)- The process of clotting that involves a series of reactions that eventually lead to the production of fibrin threads that serve to reinforce the platelet plug and trap red blood cells.
 - Thrombosis- clotting in an unbroken vessel

When blood is allowed to remain stagnant in the blood vessels or sit in a test tube, it becomes a gel (**clot, thrombus**) that separates from the liquid (**plasma**).



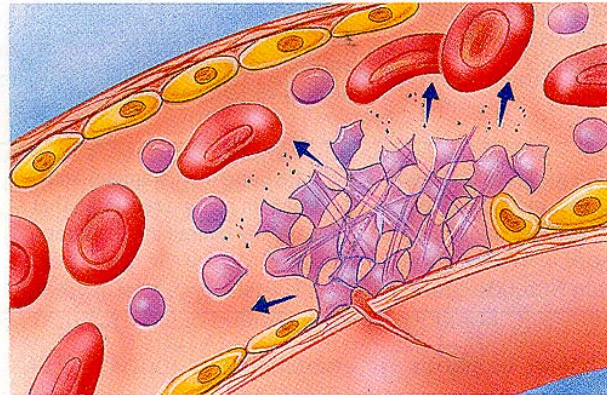
Martin M. Rotker/Science Source

Injury to the lining of the blood vessels exposes collagen fibers; platelets adhere and get sticky



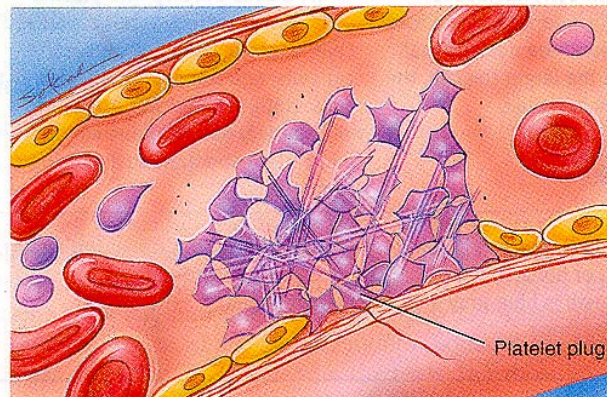
1 Platelets stick to wound inside blood vessel

Platelets release substances that causes the vessel to contract. Sticky platelets form a plug and initiate the formation of a fibrin clot



2 Platelets activate other platelets

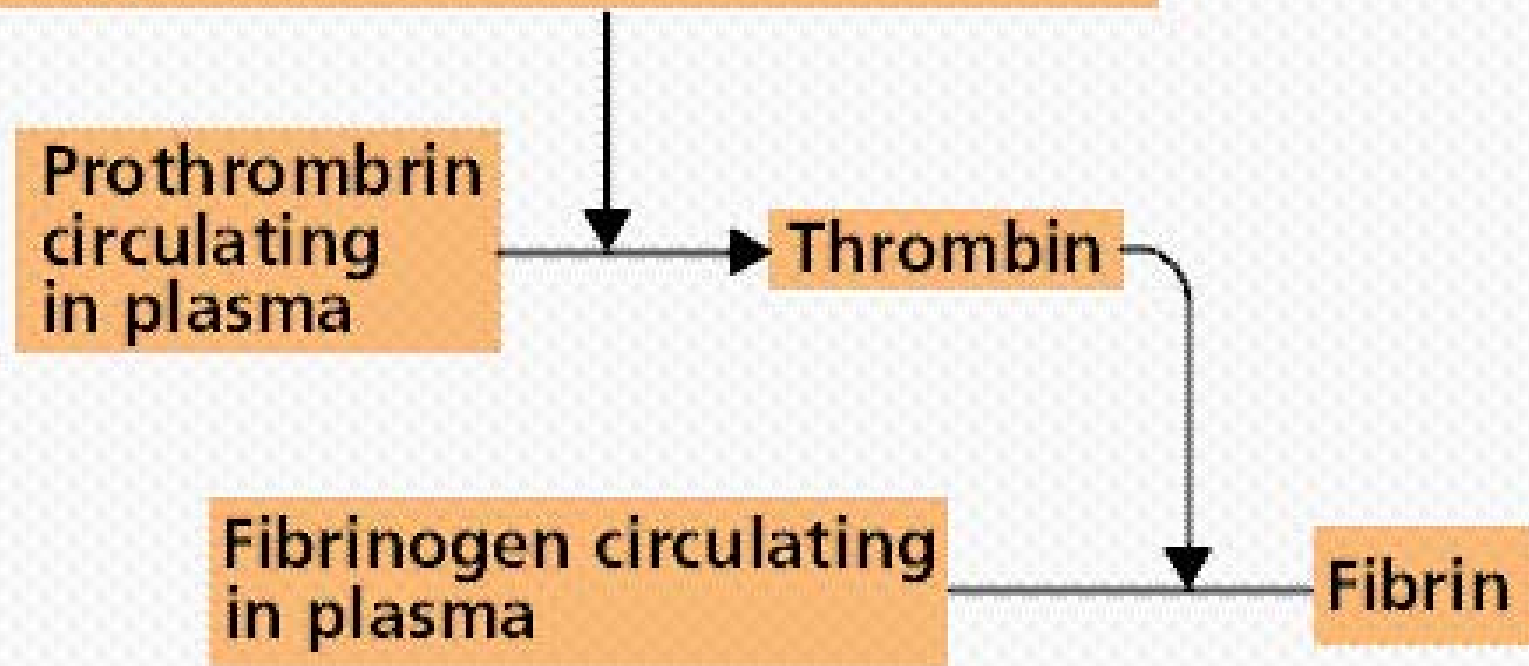
The fibrin seals the wound until the vessel wall heals



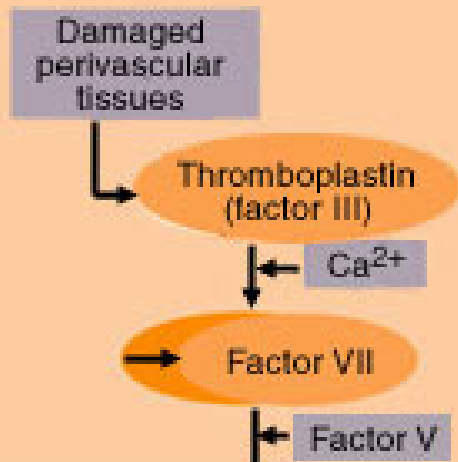
3 Platelets form plug

Clotting factors

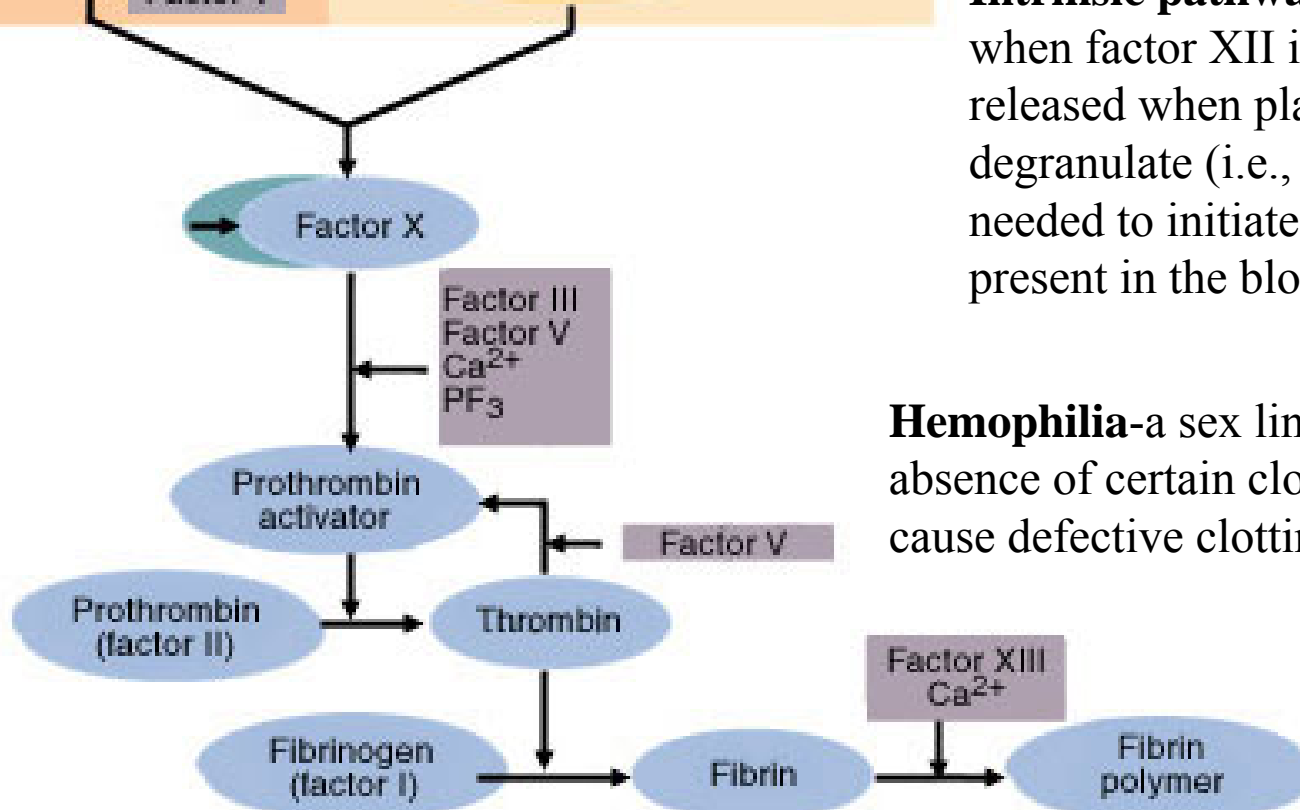
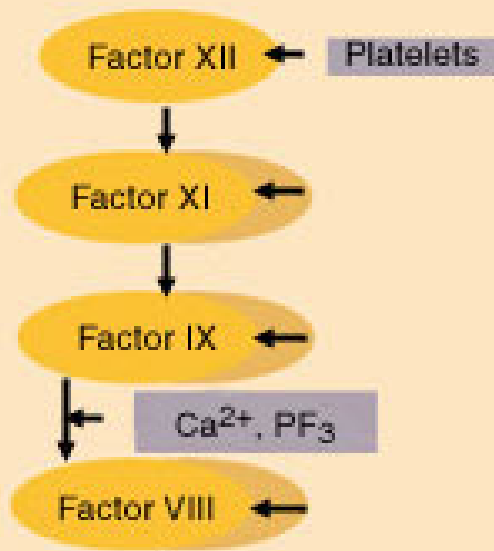
1. Released from platelets and injured tissue
2. Plasma proteins synthesized in liver and circulating in inactive form



Extrinsic mechanism



Intrinsic mechanism



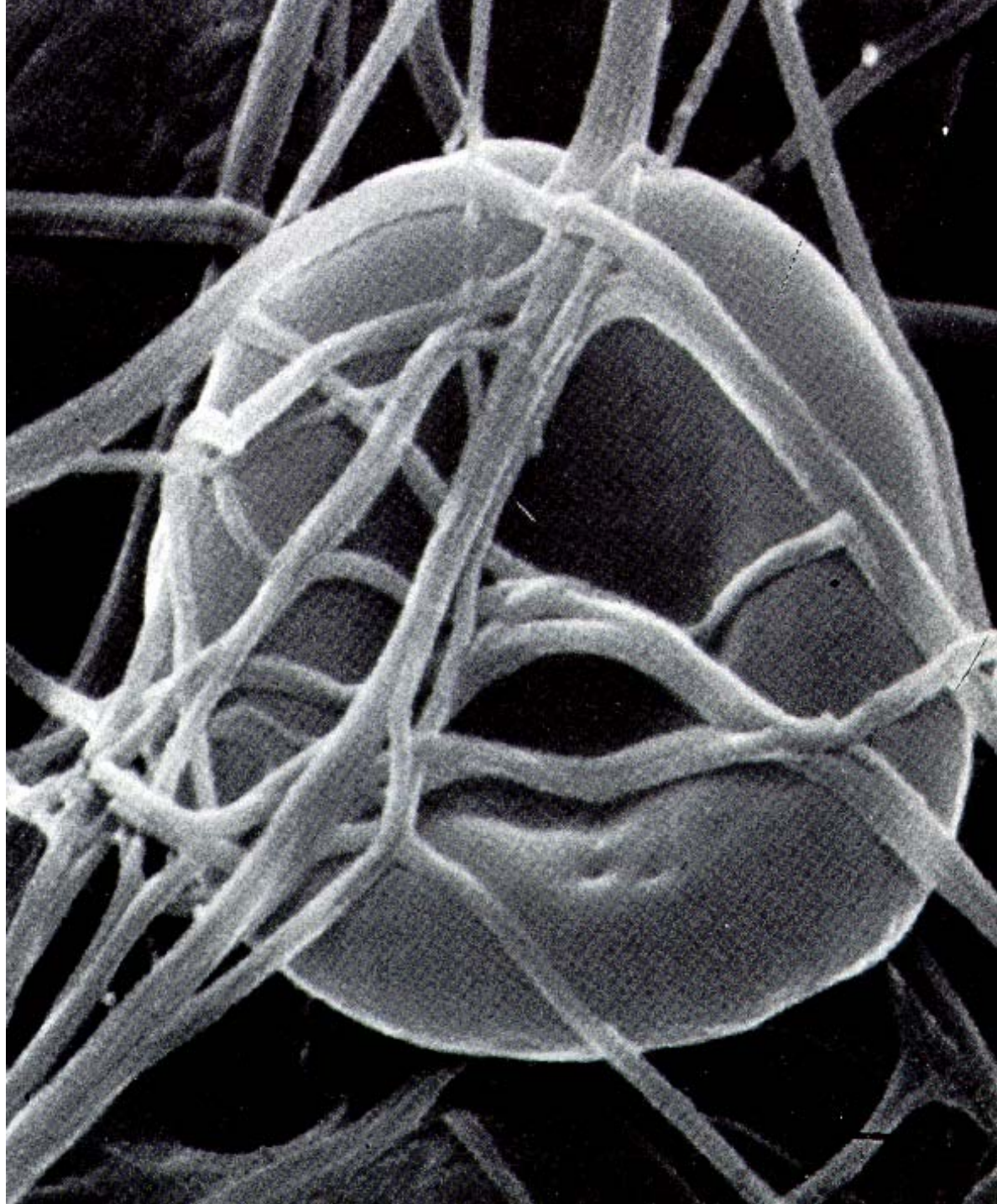
Clot Formation

Stage I can be activated in two ways:

Extrinsic pathway is initiated when clotting factors are released by the damaged blood vessel and perivascular tissue (i.e., the factors come from sources other than the blood).

Intrinsic pathway is initiated when factor XII is activated or released when platelets degranulate (i.e., everything needed to initiate the pathway is present in the blood or platelets).

Hemophilia-a sex linked hereditary absence of certain clotting factors that cause defective clotting.



Hemostasis (cont.)

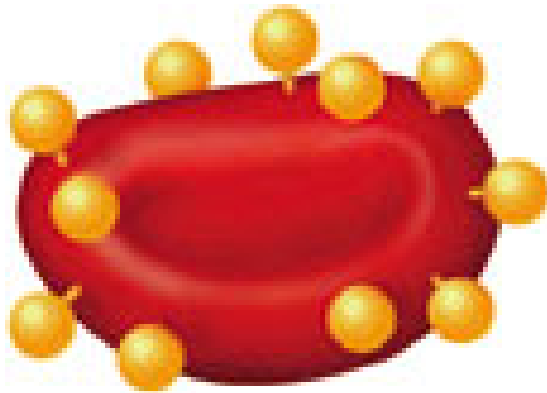
- **Clot Retraction**- the tightening of the fibrin clot that results in the pulling of the damaged blood vessels closer together.
- **Fibrinolysis**- breaking up of the clot.
 - **plasminogen** (inactive enzyme) is incorporated into the initial clot
 - blood and body tissues release substances that convert plasminogen to **plasmin** (activated plasminogen)
 - plasmin dissolves clot by digesting fibrin
- **Anticoagulants**- substances that prevent clotting
 - **heparin**- anticoagulant produced by the mast cells, basophils, and endothelial cells lining the blood vessels.
- **Thrombus**- clotting in an undamaged vessel that can block circulation. It also can dislodge and travel down stream (**embolus**).

Vitamin K and calcium are needed for formation. Vit. K is essential for the production of prothrombin and certain coagulation factors.

It is normally produced by bacteria in the large intestine.

Erythrocytes

Antigen A



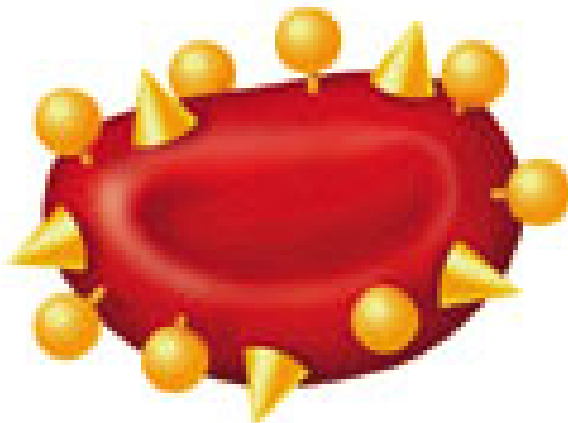
Blood Type A

Antigen B



Blood Type B

Antigen A and B

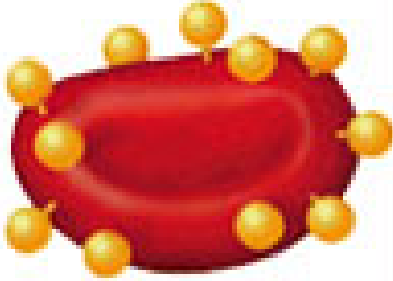
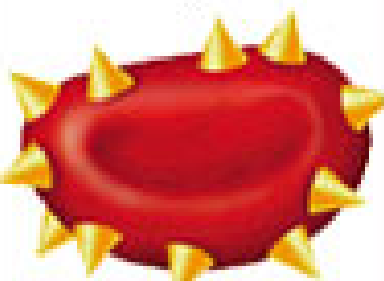
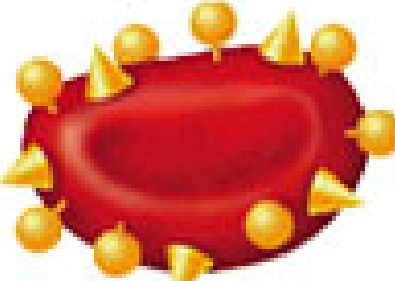

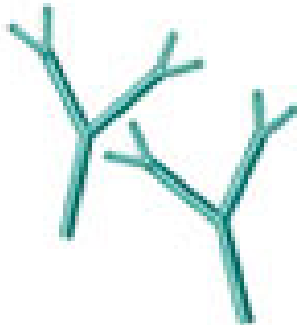




Blood Type AB

Neither antigen
A nor B



Blood Type O

Erythrocytes	Antigen A 	Antigen B 	Antigen A and B 	Neither antigen A nor B 
Plasma	Antibody B 	Antibody A 	Neither antibody A nor B	Antibody A and B 
	Type A Erythrocytes with type A surface antigens and plasma with type B antibodies	Type B Erythrocytes with type B surface antigens and plasma with type A antibodies	Type AB Erythrocytes with both type A and type B surface antigens, and neither type A nor type B plasma antibodies	Type O Erythrocytes with no ABO surface antigens, but both A and B plasma antibodies

ABO Blood Grouping

BLOOD TYPE

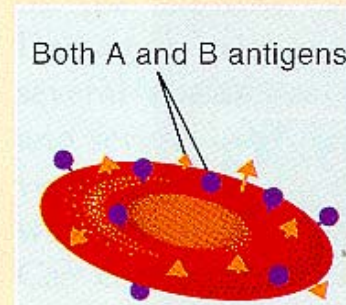
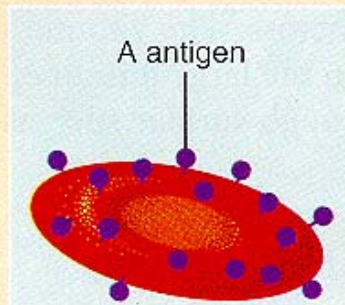
TYPE A

TYPE B

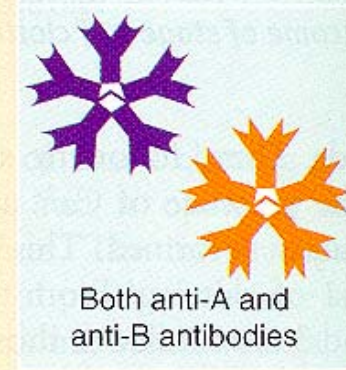
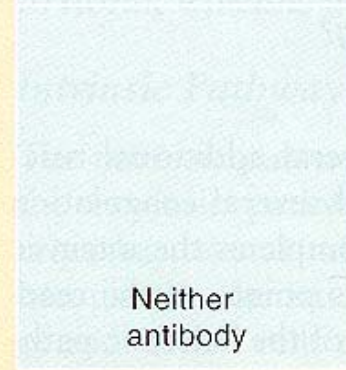
TYPE AB

TYPE O

Red blood cells



Plasma



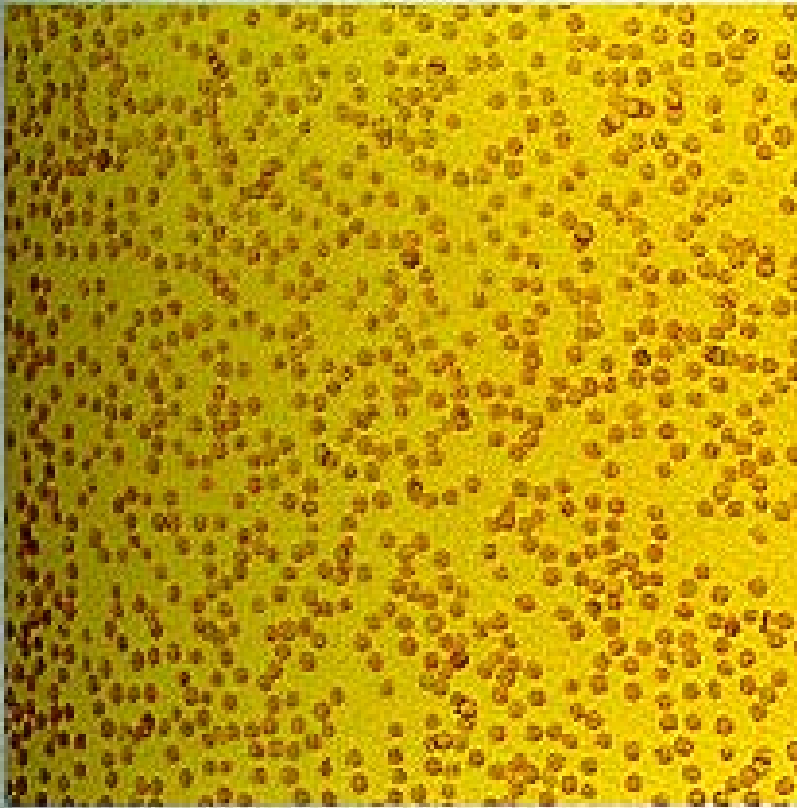
Isoantigens (agglutinogens)

Isoantibodies (agglutinins)

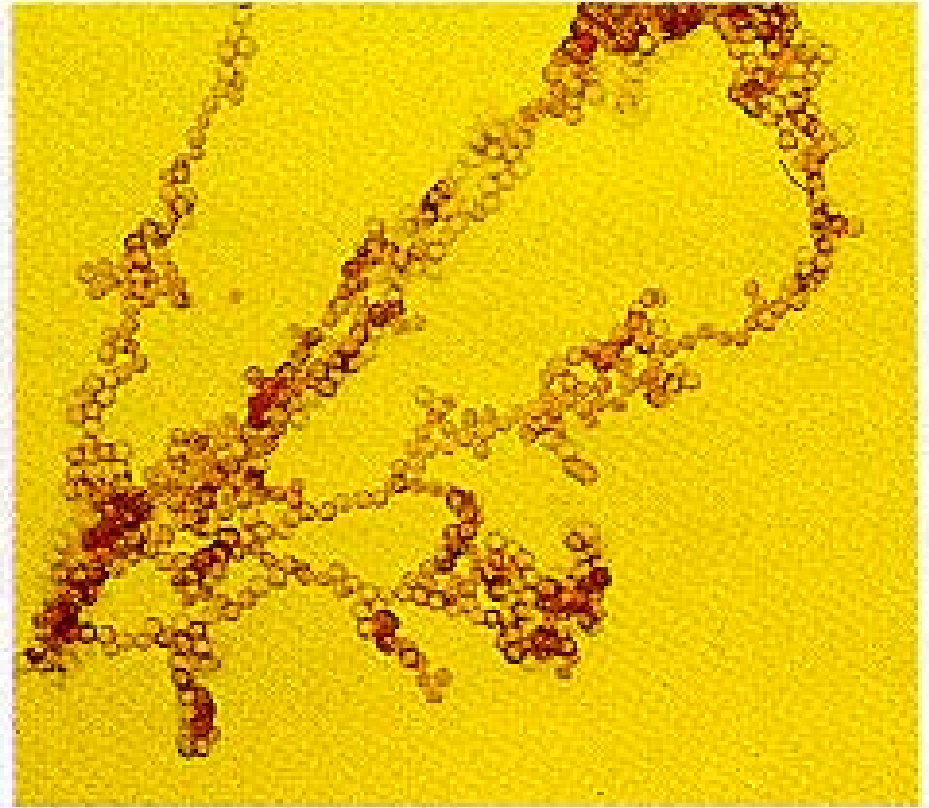
Transfusions

Agglutinate

Hemolysis



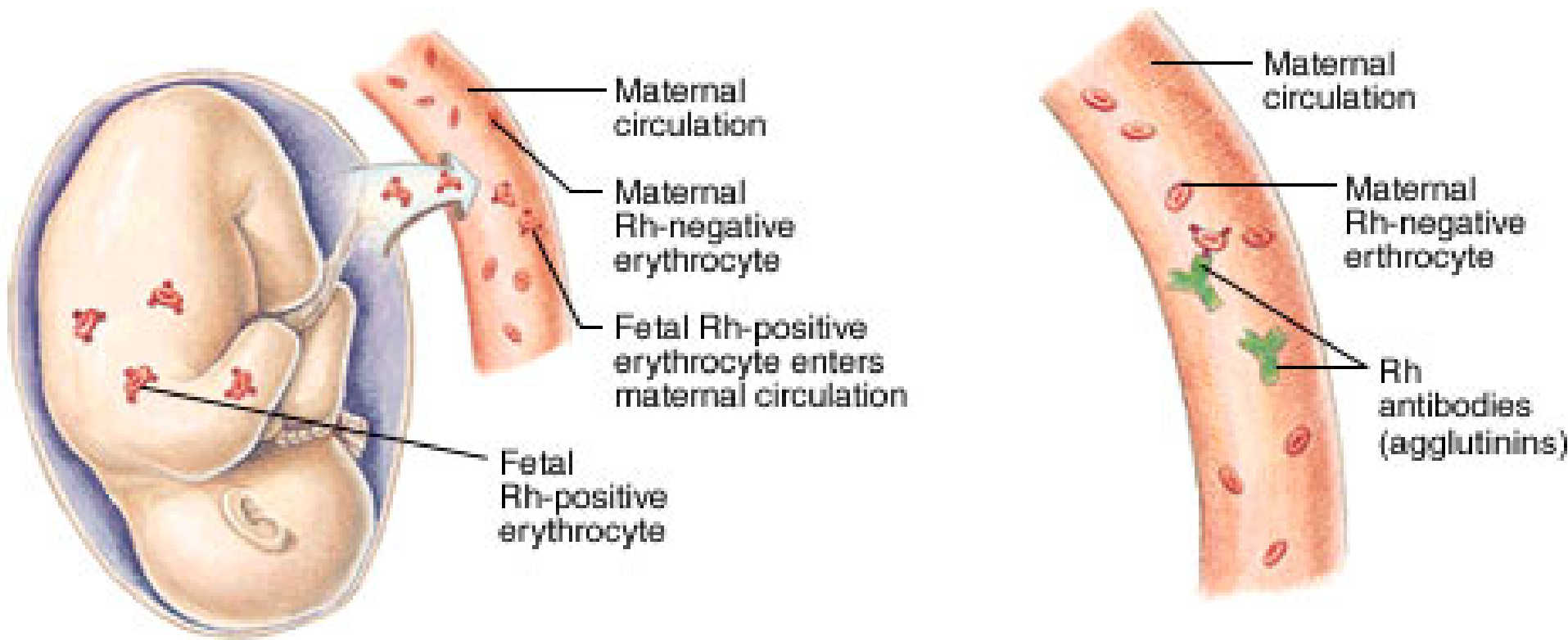
(a) Normal



(b) Agglutinated

Rh system

Hemolytic disease of the newborn (Erythroblastosis fetalis)- occurs with an Rh^- mother and a Rh^+ fetus



Hemolytic Disease of the Newborn (HDN)

Before or during delivery, Rh-positive erythrocytes from the fetus enter the blood of an Rh-negative woman through a tear in the placenta.

The mother is sensitized to the Rh antigen and produces Rh antibodies. Because this usually happens after delivery, there is no effect on the fetus in the first pregnancy.



Click on the frames above to view the animation.